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09/898,885

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65949

# SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: MOLLY CEPERLEY Examiner #: 57157 Date: 05/05/02  
Art Unit: 1641 Phone Number 308-4239 Serial Number: 09/898,885  
Mail Box and Bldg/Room Location: CM1-8 DYS Results Format Preferred (circle) PAPER DISK E-MAIL  
EXHIBIT 7E12

If more than one search is submitted, please prioritize searches in order of need. MEJ

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Dye-azide compounds for dual phototherapy

Inventors (please provide full names): Raghavan Rajagopalan, Joseph E. Bugay, Richard Dorshaw, Samuel I. Achilefu

Earliest Priority Filing Date: 07/03/01

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

① Please search for the compounds of claim 1 by searching for each (also HYPOCRELLIN dye of claim 2) type of generic dye listed, in combination with the terms AZIDE, AZIDES, or AZIDO (this is the N<sub>3</sub> term) or NITRENE or SINGLET OXYGEN.

② Please search for the dyes of claim 1 in combination with each of the E definitions of claim 2.

Point of Contact  
Susan Hanley  
Technical Info. Specialist  
CM1 6805 Tel: 305-4053

RECEIVED  
MAY 3 2 2002

NITRENE  
③ Please search for AZIDES, AZIDE, or AZIDO in combination with terms NECROSIS, APOPTOSIS (claim 34), PHOTSENSIT<sup>?</sup>, PHOTODYNAMIC, SINGLET OXYGEN.

Terms:

(PDT)  
photodynamic therapy, photosensitization, phototherapeutic, Type 1, Type 2 (claim 3)  
phototherapy

## STAFF USE ONLY

Searcher: Hanley

Searcher Phone #: \_\_\_\_\_

Searcher Location: \_\_\_\_\_

Date Searcher Picked Up: 5/7

Date Completed: 5/12/02

Searcher Prep & Review Time: \_\_\_\_\_

Clerical Prep Time: \_\_\_\_\_

Online Time: \_\_\_\_\_

## Type of Search

NA Sequence (#) \_\_\_\_\_

AA Sequence (#) \_\_\_\_\_

Structure (#) \_\_\_\_\_

Bibliographic X

Litigation \_\_\_\_\_

Fulltext \_\_\_\_\_

Patent Family \_\_\_\_\_

Other \_\_\_\_\_

## Vendors and cost where applicable

STN \_\_\_\_\_

Dialog \_\_\_\_\_

Questel/Orbit \_\_\_\_\_

Dr.Link \_\_\_\_\_

Lexis/Nexis \_\_\_\_\_

Sequence Systems \_\_\_\_\_

WWW/Internet \_\_\_\_\_

Other (specify) \_\_\_\_\_

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(FILE 'HOME' ENTERED AT 15:56:23 ON 12 MAY 2002)

FILE 'HCAPLUS' ENTERED AT 15:56:31 ON 12 MAY 2002

L1 345 S RAJAGOPALAN R?/AU  
 L2 49 S BUGAJ J?/AU  
 L3 48 S DORSHOW R?/AU  
 L4 44 S ACHILEFU S?/AU  
 L5 415 S L1-4  
 L6 93766 S ?AZIDE?  
 L7 5 S L5 AND L6  
 L8 16 S L5 AND PHOTO?  
 L9 6 S L8 AND DYE?  
 SELECT RN L7 1-5

FILE 'REGISTRY' ENTERED AT 16:01:52 ON 12 MAY 2002

L10 68 S E1-68

FILE 'HCAPLUS' ENTERED AT 16:02:02 ON 12 MAY 2002

L11 5 S L10 AND L7  
 SELECT RN L9 1-6

FILE 'REGISTRY' ENTERED AT 16:07:25 ON 12 MAY 2002

L12 64 S E69-132

FILE 'HCAPLUS' ENTERED AT 16:08:37 ON 12 MAY 2002

L13 5 S L12 AND L9  
 L14 6 S L13 OR L9

FILE 'REGISTRY' ENTERED AT 16:10:49 ON 12 MAY 2002

E AZID/CN

L15 24 S E8-37  
 L16 16 S "AZIDE" AND L15  
 L17 8 S L15 NOT L16  
 SELECT L16 RN 1-16  
 L18 545 S "AZID"

FILE 'HCAPLUS' ENTERED AT 16:22:09 ON 12 MAY 2002

L19 3867 S L16  
 L20 36392 S L18  
 L21 141428 S (N3 OR ?AZID? OR NITRENE OR SINGLET OXYGEN)  
 L22 2611 S DYE(L)L19-21  
 L23 191092 S ?CYANIN? OR ?RHODAMIN? OR ?PHENOXAZIN? OR ?PHENOTHIZIN? OR ?P  
 L24 586 S L22(L)L23  
 L25 1965 S RECEPTOR(3A) (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN  
 L26 0 S L24 AND L25  
 L27 13956 S RECEPTOR(5A) (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN  
 L28 0 S L24 AND L27  
 L29 163257 S (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN  
 L30 1 S L29 AND L24  
 L31 90 S L27 AND L23  
 L32 1 S L21 AND L31  
 L33 2 S L30 OR L32 2 cites  
 L34 88 S L27 AND L21  
 L35 1 S L34 AND L23  
 L36 0 S L35 NOT L33  
 L37 0 S L34 AND DYE  
 L38 4 S L22 AND L29 4 cites  
 L39 53 S L27(L)L23

*Inventor search*

L40 55 S L19-21(L)L27  
 L41 0 S L39 AND L40  
 L42 0 S L39 AND ?AZID?  
 L43 1 S L40 AND DYE *1 cite*  
 L44 318 S HYPOCRELLIN?  
 L45 5 S L22 AND L44  
 L46 65735 S HYPOCRELLIN? OR AZO OR METHINE OR INDOLENIUM  
 L47 429 S L22 AND L46  
 L48 429 S L47 AND DYE  
 L49 0 S L48 AND L25  
 L50 1 S L48 AND L29  
 L51 345 S L22(L)L46  
 L52 1 S L51 AND L29  
 L53 5 S L51 AND CONJUGAT?  
 L54 0 S L51 AND RECEPTOR  
 L55 11 S L50 OR L52 OR L45 OR L53  
 L56 11 S L55 NOT L13-14 *11 cites*  
 L57 9 S L39 AND PATENT/DT  
 L58 9 S L57 AND PRD<20010307  
 L59 44 S L39 NOT L57  
 L60 43 S L59 AND PD<20010307  
 L61 52 S L58 OR L60 *52 cites*  
 L62 3 S L40(L)CONJUGAT?  
 L63 3 S L40 AND CONJUGAT?  
 L64 24 S L40 AND (COVALENT? OR BOND? OR LINK?)  
 L65 27 S L62-64 *27 cites*  
 L66 3966 S L21 AND (L23 OR L46)  
 L67 28 S L66 AND L29  
 L68 26 S L67 NOT (L65 OR L61 OR L50 OR L45 OR L32-33 OR L38 OR L35)  
 L69 7 S L68 AND (CONJUGAT? OR RECEPTOR) *7 cites*  
 L70 19 S L68 NOT L69 *19 cites*  
 L71 134858 S N3 OR ?AZID? OR NITRENE OR N3  
 L72 186373 S NECROSIS OR APOPTOSIS OR PHOTOLENIT? OR PHOTODYNAMIC? OR SINGL  
 L73 1623 S L71 AND L72  
 L74 568 S L73 AND (AZIDE OR NITRENE)  
 L75 429 S L72(L) (AZIDE OR NITRENE)  
 L76 154 S L72(5A) (AZIDE OR NITRENE)  
 L77 27 S L76 AND (L23 OR L26)  
 L78 27 S L77 NOT (L65 OR L61 OR L50 OR L45 OR L32-33 OR L38 OR L35) *27 cites*

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L15 24 SEA FILE=REGISTRY ABB=ON PLU=ON (AZIDE/CN OR "AZIDE (H(N3)21-)/CN OR "AZIDE (H(N3)21-), TETRAPHENYLPHOSPHONIUM"/CN OR "AZIDE (N3-)/CN OR "AZIDE DIBENZYLDMETHYLAMMONIUM"/CN OR "AZIDE ION"/CN OR "AZIDE ION(1-)/CN OR "AZIDE RADICAL"/CN OR "AZIDE(1-)/CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3-OOXOCTADECAOXOCTADECAVANADATE(10-) (1:1)/CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3-OOXOCTADECAOXOCTADECAVANADATE(13-) (1:1)/CN OR "AZIDE, LABELED WITH NITROGEN-15"/CN OR "AZIDE, MONOHYDRATE"/CN OR AZIDE-1-15N/CN OR AZIDE-15N2/CN OR AZIDE-15N3/CN OR AZIDE-2-15N/CN OR AZIDIAMANTANE/CN OR "AZIDIC ACID"/CN OR AZIDIN/CN OR AZIDIN-NAGANIN/CN OR AZIDINE/CN OR "AZIDINE FAST SCARLET 4BS"/CN OR "AZIDINE FAST SCARLET 7BS"/CN OR "AZIDINE FAST SCARLET GGS"/CN OR "AZIDINE YELLOW 5G"/CN OR AZIDIOL/CN OR AZIDITHION/CN OR AZIDO/CN OR "AZIDO RADICAL"/CN)

L16 16 SEA FILE=REGISTRY ABB=ON PLU=ON "AZIDE" AND L15

L18 545 SEA FILE=REGISTRY ABB=ON PLU=ON "AZID"

L19 3867 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

L20 36392 SEA FILE=HCAPLUS ABB=ON PLU=ON L18

L21 141428 SEA FILE=HCAPLUS ABB=ON PLU=ON (N3 OR ?AZID? OR NITRENE OR SINGLET OXYGEN)

L22 2611 SEA FILE=HCAPLUS ABB=ON PLU=ON DYE(L) (L19 OR L20 OR L21)

L23 191092 SEA FILE=HCAPLUS ABB=ON PLU=ON ?CYANIN? OR ?RHODAMIN? OR ?PHENOXAZIN? OR ?PHENOTHIZIN? OR ?PHENOSELENAZIN? OR ?FLUORESCIN? OR ?PORPHYRIN? OR ?BENZOPORPHYRIN? OR ?SQUARAIN? OR ?CORRIN? OR ?COROCONIUM? OR AZO(W)DYE OR METHIN?(W)DYE OR INDOLENIUM(W)DYE

L24 586 SEA FILE=HCAPLUS ABB=ON PLU=ON L22(L) L23

L27 13956 SEA FILE=HCAPLUS ABB=ON PLU=ON RECEPTOR(5A) (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)

L29 163257 SEA FILE=HCAPLUS ABB=ON PLU=ON (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)

L30 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L24

L31 90 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L23

L32 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 AND L31

L33 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 OR L32

*various azides from Reg*

*L32 cite is same as #1 of L33*

*L33 consists of azide & dyes of cl 1 & the molecules of cl 2 (receptor is not included)*



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L33 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:314927 HCAPLUS

DOCUMENT NUMBER: 132:319503

TITLE: Screening for analytes using labeled receptors

INVENTOR(S): Viel, Gerhard Theodoor; Ensing, Kornelis

PATENT ASSIGNEE(S): Elimo B.V., Neth.

SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000026674	A1	20000511	WO 1998-NL629	19981030
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9911778	A1	20000522	AU 1999-11778	19981030
EP 1125132	A1	20010822	EP 1998-954828	19981030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: WO 1998-NL629 A 19981030

AB A method for assaying an analyte in a sample comprises (a) contacting the sample with material comprising a receptor which is present in a liposome and which liposome comprises a detectable functionality, said contact occurring under conditions resulting in binding of the receptor to analyte if present before or concomitant with step b, wherein step (b) consists of contacting the sample with an immobilized ligand for the receptor said contact occurring under conditions resulting in binding of the receptor to the ligand, with steps a and b being followed by (c) sepg. the resulting immobilized ligand-receptor fraction and the receptor fraction present in soln. and (d) assaying the detectable functionality of the receptor in a fraction from step (c) in a manner known per se for its detection. Suitably the receptor is present in step (a) in a concn. between 1 pM - 1 nM and the detectable functionality in step (a) is present in a concn. of 1 pM - 1 .mu.M and the immobilized ligand in step (b) has a Kd for the receptor <50 nM. The immobilized ligand should be present in an amt. required to capture 10-99 % of the receptors in the assay in the absence of analyte at a receptor concn. below the Kd of the immobilized ligand and receptor under conditions otherwise corresponding to those of the assay. The conditions and the detectable functionalities being selected such that a 0.1-10 % change in either the ligand-receptor fraction or in the free receptor fraction can be qual. or quant. detectable. Benzodiazepine was immobilized in wells of a microtiter plate. Proteoliposomes contg. calf benzodiazepine receptors and labeled with **fluorescein**-DHPE were used in the assay.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L33 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS  
 IC ICM G01N033-58  
 ICS G01N033-566; G01N033-567; G01N033-543; G01N033-74  
 CC 9-2 (Biochemical Methods)  
 Section cross-reference(s): 1  
 ST labeled receptor liposome immobilized ligand assay; benzodiazepam receptor  
 fluorescence liposome assay  
 IT Detergents  
 (anionic; screening for analytes using labeled receptors)  
 IT Microtiter plates  
 (benzodiazepine deriv. immobilized on; screening for analytes using  
 labeled receptors)  
 IT Detergents  
 (cationic; screening for analytes using labeled receptors)  
 IT Chemoreceptors  
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical  
 study); BIOL (Biological study); USES (Uses)  
 (chemotactic; screening for analytes using labeled receptors)  
 IT Ligands  
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical  
 study); BIOL (Biological study); USES (Uses)  
 (immobilized; screening for analytes using labeled receptors)  
 IT Enzymes, biological studies  
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical  
 study); BIOL (Biological study); USES (Uses)  
 (in liposomes; screening for analytes using labeled receptors)  
 IT Lipids, biological studies  
 Receptors  
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical  
 study); BIOL (Biological study); USES (Uses)  
 (labeled; screening for analytes using labeled receptors)  
 IT Detergents  
 (nonionic; screening for analytes using labeled receptors)  
 IT Membranes, nonbiological  
 (receptor bound to; screening for analytes using labeled receptors)  
 IT Liposomes  
 (receptor in; screening for analytes using labeled receptors)  
 IT Chemiluminescence spectroscopy  
 Detergents  
 Drug screening  
 Fluorometry  
 Test kits  
 (screening for analytes using labeled receptors)  
 IT 5-HT receptors  
 Adenosine receptors  
 Adrenoceptors  
 Androgen receptors  
 Benzodiazepine receptors  
 Calcium channel  
 Cannabinoid receptors  
 Cholecystokinin receptors  
 Cytokine receptors  
 Dopamine receptors  
 Epidermal growth factor receptors  
 Estrogen receptors  
 GABA receptors  
 Glucocorticoid receptors  
 Glycine receptors  
 Histamine receptors

Leukotriene receptors  
 Muscarinic receptors  
 Nicotinic receptors  
 Opioid receptors  
 Progesterone receptors  
 Reagents  
 Sodium channel  
     **Steroid receptors**  
 Tachykinin receptors  
 RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
     (screening for analytes using labeled receptors)  
 IT Glycolipids  
     Phospholipids, analysis  
     RL: ARU (Analytical role, unclassified); ANST (Analytical study)  
         (screening for analytes using labeled receptors)  
 IT Detergents  
     (zwitterionic; screening for analytes using labeled receptors)  
 IT 161106-88-3  
     RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
         (BODIPY FL-C5-HPC; screening for analytes using labeled receptors)  
 IT 228262-70-2, **Fluorescein** DHPE  
     RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
         (**fluorescein** DHPE; screening for analytes using labeled receptors)  
 IT 846-49-1, Lorazepam  
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
         (in inhibition expts.; screening for analytes using labeled receptors)  
 IT 141-43-5, 2-Aminoethanol, reactions 1071-93-8, Adipic acid  
     **dihydrazide** 17617-59-3, Didesethylflurazepam 25952-53-8,  
     1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride  
     RL: RCT (Reactant); RACT (Reactant or reagent)  
         (in prepn. of microtiter plate with immobilized benzodiazepine deriv.; screening for analytes using labeled receptors)  
 IT 9003-53-6D, Polystyrene, maleic anhydride-activated  
     RL: DEV (Device component use); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)  
         (microtiter plate, benzodiazepine deriv. immobilization on; screening for analytes using labeled receptors)  
 IT 12794-10-4, Benzodiazepine  
     RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
         (screening for analytes using labeled receptors)  
 IT 9001-66-5, Monoamine oxidase 9001-78-9 9014-00-0, Luciferase  
     12794-10-4D, Benzodiazepine, derivs., immobilized 57093-06-8, Dansyl DHPE  
     RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
         (screening for analytes using labeled receptors)  
 IT 57-88-5, Cholesterol, analysis  
     RL: ARU (Analytical role, unclassified); ANST (Analytical study)  
         (screening for analytes using labeled receptors)  
 IT 80573-68-8  
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
         (screening for analytes using labeled receptors)

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L33 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:577151 HCAPLUS  
 DOCUMENT NUMBER: 115:177151  
 TITLE: Evaluation of the newborn mouse model for chemical tumorigenesis  
 AUTHOR(S): Fujii, Keiji  
 CORPORATE SOURCE: Inst. Basic Med. Sci., Univ. Tsukuba, Tsukuba, 305, Japan  
 SOURCE: Carcinogenesis (London) (1991), 12(8), 1409-15  
 CODEN: CRNGDP; ISSN: 0143-3334  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB A total of 45 chems., including 2 arom. hydrocarbons, 5 arom. amines, 3 **azo dyes**, 10 nitroso compds., 3 **steroids**, 4 tryptophan metabolites and their related compds., 4 naturally occurring substances, 4 pyrolyzates of amino acids, and 10 misc. compds., were tested for newborn mouse tumorigenesis assay (NMTA). The results of the NMTA were compared with data from Survey of Compds. Which Have Been Tested for Carcinogenic Activity, NIH, NCI, USA (SCWHBTCA), and also with data from the IARC Monographs (Vols 1-41), Lyon, France (IARC). Of the 45 chems. tested by the NMTA, 28 chems. showed pos. results in the NMTA, and the remaining 17 chems. were neg. for tumor development. The correlation of the results between the NMTA and the mouse and/or rat carcinogenesis test starting at young adult age reported in the SCWHBTCA and in the IARC were compared with 37 chems. tested; the remaining 8 chems. were found only in NMTA results. Therefore, 31 of 37 chems. (83.8%) tested by the NMTA showed similar carcinogenic or non-carcinogenic results obtained in adult mouse and/or rat carcinogenesis tests. The remaining 6 chems. showed contradictory results between the NMTA and adult mouse and/or rat carcinogenesis tests. Those 6 chems. were N-hydroxy-4-acetylaminobiphenyl, estradiol, 3-hydroxyanthranilic acid, 3-hydroxy-L-kynurenine, isonicotinic acid **hydrazide**, and phenobarbital. Among the 37 chems., 34 were comparable with the results of the adult mouse carcinogenesis test and those of the NMTA. Twenty-nine of 34 chems. (85.3%) showed similar results to the adult mouse carcinogenesis test. Contradictory results were obtained with the following 5 chems.: N-hydroxyacetylaminobiphenyl, 3-hydroxyanthranilic acid, 3-hydroxy-L-kynurenine, isonicotinic acid **hydrazide** and phenobarbital. There were 35 chems. which were comparable with the results of the adult rat carcinogenesis test, and 32 chems. showed the same results as the NMTA (91.4%). Dissimilar results were obtained with the following 3 chems.: estradiol, 3-hydroxyanthranilic acid and phenobarbital. Thus, the NMTA is one of the most useful and reliable methods for detecting tumorigenic or non-tumorigenic chems., when a small amt. of chem. is available for rodent carcinogenesis test and the duration of the study is limited to 1 yr.

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L15 24 SEA FILE=REGISTRY ABB=ON PLU=ON (AZIDE/CN OR "AZIDE (H(N3)21-)" /CN OR "AZIDE (H(N3)21-), TETRAPHENYLPHOSPHONIUM"/CN OR "AZIDE (N3-)" /CN OR "AZIDE DIBENZYLDMETHYLAMMONIUM"/CN OR "AZIDE ION"/CN OR "AZIDE ION(1-)" /CN OR "AZIDE RADICAL"/CN OR "AZIDE(1-)" /CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3- OXOOCTADECAXOOCTADECANADATE(10-) (1:1)" /CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3- OXOOCTADECAXOOCTADECANADATE(13-) (1:1)" /CN OR "AZIDE, LABELED WITH NITROGEN-15"/CN OR "AZIDE, MONOHYDRATE"/CN OR AZIDE-1-15N/CN OR AZIDE-15N2/CN OR AZIDE-15N3/CN OR AZIDE-2-15N/CN OR AZIDIAMANTANE/CN OR "AZIDIC ACID"/CN OR AZIDIN/CN OR AZIDIN-NAGANIN/CN OR AZIDINE/CN OR "AZIDINE FAST SCARLET 4BS"/CN OR "AZIDINE FAST SCARLET 7BS"/CN OR "AZIDINE FAST SCARLET GGS"/CN OR "AZIDINE YELLOW 5G"/CN OR AZIDIOL/CN OR AZIDITHION/CN OR AZIDO/CN OR "AZIDO RADICAL"/CN)

L16 16 SEA FILE=REGISTRY ABB=ON PLU=ON "AZIDE" AND L15

L18 545 SEA FILE=REGISTRY ABB=ON PLU=ON "AZID"

L19 3867 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

L20 36392 SEA FILE=HCAPLUS ABB=ON PLU=ON L18

L21 141428 SEA FILE=HCAPLUS ABB=ON PLU=ON (N3 OR ?AZID? OR NITRENE OR SINGLET OXYGEN)

L22 2611 SEA FILE=HCAPLUS ABB=ON PLU=ON DYE(L) (L19 OR L20 OR L21)

L29 163257 SEA FILE=HCAPLUS ABB=ON PLU=ON (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)

L38 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L29

azides  
from  
reg  
file

all azides from Reg file and HCAPLUS text search

L38 consists of azides linked w/ dye;  
this result is combined with the  
compounds (not as receptors) of L2

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L38 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:401195 HCAPLUS

DOCUMENT NUMBER: 117:1195

TITLE: Megestrol acetate reverses multidrug resistance and interacts with P-glycoprotein

AUTHOR(S): Fleming, Gini F.; Amato, Jacqueline M.; Agresti, Michael; Safa, Ahmad R.

CORPORATE SOURCE: Dep. Med., Univ. Chicago, Chicago, IL, 60637, USA

SOURCE: Cancer Chemother. Pharmacol. (1992), 29(6), 445-9

CODEN: CCPHDZ; ISSN: 0344-5704

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The multidrug resistance (MDR)-modulating effects of progesterone (PRG) and an orally active, structurally related compd., megestrol acetate (MA), were examd. in several MDR human cell lines. At 100 .mu.M, both **steroids** inhibited the binding of a Vinca alkaloid photoaffinity analog to P-glycoprotein (P-gp) in MDR human neuroblastic SH-SY5Y/VCR cells [which show >1500-fold resistance to vincristine (VCR) in the tetrazolium **dye** (MTT) assay]. However, 100 .mu.M MA markedly enhanced the binding of [3H]**azidopine** to P-gp in both SH-SY5Y/VCR cells and the MDR human epidermoid KB-GSV2 cell line (which displays 250-fold resistance to VCR in the MTT assay). PRG had little effect on the binding of [3H]**azidopine** to P-gp. MA at low doses was more effective than PRG in sensitizing cells to VCR and enhancing their accumulation of [3H]VCR. The highly resistant SH-SY5Y/VCR subline exhibited significant collateral sensitivity to both **steroids**. Apparently, MA may be a clin. useful modulator of MDR.

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L38 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:577151 HCAPLUS  
 DOCUMENT NUMBER: 115:177151  
 TITLE: Evaluation of the newborn mouse model for chemical tumorigenesis  
 AUTHOR(S): Fujii, Keiji  
 CORPORATE SOURCE: Inst. Basic Med. Sci., Univ. Tsukuba, Tsukuba, 305, Japan  
 SOURCE: Carcinogenesis (London) (1991), 12(8), 1409-15  
 CODEN: CRNGDP; ISSN: 0143-3334  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB A total of 45 chems., including 2 arom. hydrocarbons, 5 arom. amines, 3 azo **dyes**, 10 nitroso compds., 3 **steroids**, 4 tryptophan metabolites and their related compds., 4 naturally occurring substances, 4 pyrolyzates of amino acids, and 10 misc. compds., were tested for newborn mouse tumorigenesis assay (NMTA). The results of the NMTA were compared with data from Survey of Compds. Which Have Been Tested for Carcinogenic Activity, NIH, NCI, USA (SCWHBTCA), and also with data from the IARC Monographs (Vols 1-41), Lyon, France (IARC). Of the 45 chems. tested by the NMTA, 28 chems. showed pos. results in the NMTA, and the remaining 17 chems. were neg. for tumor development. The correlation of the results between the NMTA and the mouse and/or rat carcinogenesis test starting at young adult age reported in the SCWHBTCA and in the IARC were compared with 37 chems. tested; the remaining 8 chems. were found only in NMTA results. Therefore, 31 of 37 chems. (83.8%) tested by the NMTA showed similar carcinogenic or non-carcinogenic results obtained in adult mouse and/or rat carcinogenesis tests. The remaining 6 chems. showed contradictory results between the NMTA and adult mouse and/or rat carcinogenesis tests. Those 6 chems. were N-hydroxy-4-acetylaminobiphenyl, estradiol, 3-hydroxyanthranilic acid, 3-hydroxy-L-kynurenine, isonicotinic acid **hydrazide**, and phenobarbital. Among the 37 chems., 34 were comparable with the results of the adult mouse carcinogenesis test and those of the NMTA. Twenty-nine of 34 chems. (85.3%) showed similar results to the adult mouse carcinogenesis test. Contradictory results were obtained with the following 5 chems.: N-hydroxyacetylaminobiphenyl, 3-hydroxyanthranilic acid, 3-hydroxy-L-kynurenine, isonicotinic acid **hydrazide** and phenobarbital. There were 35 chems. which were comparable with the results of the adult rat carcinogenesis test, and 32 chems. showed the same results as the NMTA (91.4%). Dissimilar results were obtained with the following 3 chems.: estradiol, 3-hydroxyanthranilic acid and phenobarbital. Thus, the NMTA is one of the most useful and reliable methods for detecting tumorigenic or non-tumorigenic chems., when a small amt. of chem. is available for rodent carcinogenesis test and the duration of the study is limited to 1 yr.



=> d ibib abs 3

L38 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1968:75658 HCAPLUS

DOCUMENT NUMBER: 68:75658

TITLE: Fluorescence histochemistry. III. Demonstration with salicyl hydrazide of the aldehydes present in periodate-oxidized mucosubstances

AUTHOR(S): Stoward, Peter J.

CORPORATE SOURCE: Dep. Human Anat., Oxford, Engl.

SOURCE: J. R. Microsc. Soc. (1967), 87(Pt. 2), 247-57

CODEN: JRMSAS

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Salicyl **hydrazide** forms blue fluorescent derivs. with all potentially Schiff-reactive, periodateoxidized mucosubstances in fixed tissue sections. The derivs. formed from sulfo- and sialomucins usually emit an intense fluorescence, but that emitted by neutral mucosubstance is less intense. Al salts enhance the fluorescence emitted by these derivs., but Zn salts tend to quench it. Cytoplasmic proteins emit a red or purple fluorescence after being treated with a soln. contg. a Solochrome Black **dye** (Solochrome Black AS is the most useful) and an Al salt. This fluorescence enables the blue fluorescence emitted by periodated-oxidized mucosubstance salicyl hydrazones to be seen more clearly. Salicyl **hydrazide** forms stable fluorescent products only with aldehydes, and Camber group II keto **steroids**, and is therefore highly specific. The derivs. formed with aldehydes emit an intense fluorescence which does not face noticeably on prolonged exposure to uv light, while the fluorescence of keto **steroid** salicyl hydrazones fades after about 5 min. exposure to uv light. Moreover, these aldehyde hydrazones are unique among aldehyde acid arylhydrazones because they can only be converted into formazans. 17 references.

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L38 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1950:3554 HCAPLUS

DOCUMENT NUMBER: 44:3554

ORIGINAL REFERENCE NO.: 44:726g-i,727a

TITLE: The cytology and cytochemistry of the adrenal cortex

AUTHOR(S): Greep, Roy O.; Deane, Helen Wendler

SOURCE: Ann. N.Y. Acad. Sci. (1949), 50, 596-615

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB Differences occur in the form and chromophilia of mitochondria and Golgi app. in active and inactive cortical cells. Ascorbic acid occurs as fine granules in the cells of the glomerulosa and as coarse granules in the fasciculata and reticularis. Keto **steroids** are characterized in frozen sections by reactions with Sudan **dyes**, phenylhydrazine, **semicarbazide**, Schiff reagent, and ammoniacal silver nitrate; they are birefringent, exhibit autofluorescence, and are acetone-sol. The lipide droplets of the glomerulosa and outer fasciculata give pos. tests for keto **steroids**, while the inner fasciculata and the reticularis stain only with Sudan **dyes**, and are believed to be triglycerides. Hypophysectomy results in loss of keto **steroids** from the outer fasciculata but not from the glomerulosa. In the adaptation syndrome pronounced changes occur in the fasciculata but not in the glomerulosa. The fasciculata enlarges after injections of adrenotropin with first a decline and later an increase in keto **steroid** reactions, while the glomerulosa is unchanged. Desoxycorticosterone acetate administration results in loss of lipide and keto **steroid** from the glomerulosa, but does not affect the fasciculata. Adrenal cortical exts. or 11-hydroxy corticosteroids produced loss of the keto **steroid** droplets from the fasciculata. No evidence was found for translocation of cells in the adrenal cortex. In the rat the zona-glomerulosa is autonomous and secretes desoxycorticosteroids for regulation of fluid and electrolyte balance while the fasciculata is under control of the pituitary gland and secretes the 11-oxy corticosteroids concerned with gluconeogenesis and resistance to stress.

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L15 24 SEA FILE=REGISTRY ABB=ON PLU=ON (AZIDE/CN OR "AZIDE (H(N3)21-)" /CN OR "AZIDE (H(N3)21-), TETRAPHENYLPHOSPHONIUM"/CN OR "AZIDE (N3-)" /CN OR "AZIDE DIBENZYL DIMETHYLAMMONIUM"/CN OR "AZIDE ION"/CN OR "AZIDE ION(1-)" /CN OR "AZIDE RADICAL"/CN OR "AZIDE(1-)" /CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3- OXOOCTADECAXOOCTADECANADATE(10-) (1:1)" /CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3- OXOOCTADECAXOOCTADECANADATE(13-) (1:1)" /CN OR "AZIDE, LABELED WITH NITROGEN-15"/CN OR "AZIDE, MONOHYDRATE"/CN OR AZIDE-1-15N/CN OR AZIDE-15N2/CN OR AZIDE-15N3/CN OR AZIDE-2-15N/CN OR AZIDIAMANTANE/CN OR "AZIDIC ACID"/CN OR AZIDIN/CN OR AZIDIN-NAGANIN/CN OR AZIDINE/CN OR "AZIDINE FAST SCARLET 4BS"/CN OR "AZIDINE FAST SCARLET 7BS"/CN OR "AZIDINE FAST SCARLET GGS"/CN OR "AZIDINE YELLOW 5G"/CN OR AZIDIOL/CN OR AZIDITHION/CN OR AZIDO/CN OR "AZIDO RADICAL"/CN)

L16 16 SEA FILE=REGISTRY ABB=ON PLU=ON "AZIDE" AND L15

L18 545 SEA FILE=REGISTRY ABB=ON PLU=ON "AZID"

L19 3867 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

L20 36392 SEA FILE=HCAPLUS ABB=ON PLU=ON L18

L21 141428 SEA FILE=HCAPLUS ABB=ON PLU=ON (N3 OR ?AZID? OR NITRENE OR SINGLET OXYGEN)

L27 13956 SEA FILE=HCAPLUS ABB=ON PLU=ON RECEPTOR(5A) (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)

L40 55 SEA FILE=HCAPLUS ABB=ON PLU=ON (L19 OR L20 OR L21) (L) L27

L43 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L40 AND DYE

*azides  
selected  
from  
key*

*L43 azide and any of the receptors  
that bind the cpds in Q2*

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L43 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1980:54712 HCAPLUS

DOCUMENT NUMBER: 92:54712

TITLE: Chemical compositions, their use as cytochemical agents and methods for the detection of steroid hormone receptors in human tissues

INVENTOR(S): Lee, Sin Hang

PATENT ASSIGNEE(S): USA

SOURCE: Eur. Pat. Appl., 46 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 3583	A1	19790822	EP 1979-100329	19790205
EP 3583	B1	19811202		
R: BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4215102	A	19800729	US 1979-1205	19790105
PRIORITY APPLN. INFO.:			US 1978-876564	19780210
			US 1978-947700	19780929
			US 1979-1205	19790105

AB Novel chem. compns. are provided consisting essentially of a hormone-carrier-fluorochrome conjugate, esp. an estrogen-carrier-fluorochrome or a progesterone-carrier-fluorochrome conjugate. The conjugates are cytochem. agents and can be used in a method for the detection and identification of estrogen or progesterone receptor cells in carcinomas of the breast by application of the agent to an excised unfixed frozen tissue section, which is then examd. for the appearance of fluorescent **dye** staining of the cells therein, for evaluation of potential endocrine or hormone therapy of the patient. Cytochem. agents and methods for the detection of other types of hormone receptor cells in various kinds of cancerous tissue are also disclosed, using sex hormones and endocrine steroid components.

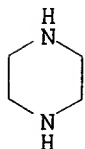
IT 110-85-0D, dioxo derivs.

RL: ANST (Analytical study)

(conjugates contg., for **steroid hormone receptors** fluorescent cytochem. detection)

RN 110-85-0 HCAPLUS

CN Piperazine (8CI, 9CI) (CA INDEX NAME)



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L43 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS

IC C07G015-00; A61K047-00; C07J001-00; G01N033-16

- CC 9-6 (Biochemical Methods)  
Section cross-reference(s): 2, 14
- ST breast carcinoma steroid hormone receptor detection; cytochem steroid hormone receptor; fluorochrome steroid conjugate cytochem; estrogen receptor cytochem; progesterone receptor cytochem
- IT Albuminoids  
Albumins  
Chromoproteins  
Globulins  
Glutelins  
Glycoproteins  
Histones  
Lipoproteins  
Mucoproteins  
Nucleoproteins  
Peptides, uses and miscellaneous  
Peptones  
Phosphoproteins  
Prolamins  
Protamines  
Proteoses  
RL: ANST (Analytical study)  
(conjugates contg., for steroid hormone receptors fluorescent cytochem. detection)
- IT Gynecomastia  
(estrogen receptors detection in, fluorescent cytochem.)
- IT Receptors  
RL: PROC (Process)  
(for steroid hormones, fluorescent cytochem. detection of, in neoplasms)
- IT Steroids, biological studies  
RL: BIOL (Biological study)  
(hormones, receptors for, fluorescent cytochem. detection of, in neoplasms)
- IT Carcinoma  
(of mammary gland, steroid hormone receptors fluorescent cytochem. detection in)
- IT Albumins, blood serum  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(reaction products with fluoroscein isothiocyanate, prepn. and reaction of, with steroid hormone derivs. for hormone receptors detection)
- IT Androgens  
Corticosteroids, biological studies  
RL: ANST (Analytical study)  
(receptors for, fluorescent cytochem. detection of, in neoplasms)
- IT Histochemistry  
(steroid hormone receptors detection in, hormone-fluorochrome conjugates for)
- IT Neoplasm  
(steroid hormone receptors of, fluorescent cytochem. detection of)
- IT Anhydrides  
RL: ANST (Analytical study)  
(cyclic, conjugates contg., for steroid hormone receptors fluorescent cytochem. detection)
- IT Adenoma  
(fibro-, estrogen receptors detection in, fluorescent cytochem.)
- IT Microscopy  
(fluorescence, in hormone receptors detection)
- IT Staining, biological  
(fluorescent, of hormone receptors)

IT Spectrochemical analysis  
(fluorometric, in cytochem., for hormone receptors detection)

IT Proteins  
RL: ANST (Analytical study)  
(metallo-, conjugates contg., for steroid hormone receptors fluorescent cytochem. detection)

IT Mammary gland  
(neoplasm, carcinoma, steroid hormone receptor of, fluorescent cytochem. detection of)

IT 60-54-8 65-61-2 81-88-9 83-89-6 135-49-9 573-58-0 1326-12-1  
1829-00-1 1837-57-6 2086-83-1 2150-33-6 2321-07-5 2390-54-7  
2465-27-2 3244-88-0 3520-42-1 5409-37-0 6232-60-6 6359-38-2  
8064-60-6 10114-41-7 10114-42-8 10181-37-0 17372-87-1 65589-70-0  
70281-37-7 72490-80-3  
RL: ANST (Analytical study)  
(conjugates contg., for steroid hormone receptor fluorescent cytochem. detection)

IT **110-85-0D**, dioxo derivs.  
RL: ANST (Analytical study)  
(conjugates contg., for **steroid hormone receptors** fluorescent cytochem. detection)

IT 3434-45-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and hydrolysis of)

IT 571-92-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and reaction of, with carboxymethoxylamine hemihydrochloride)

IT 41238-98-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and reaction of, with fluorescein isothiocyanate-serum albumin conjugate, for progesterone receptor detection)

IT 35048-47-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and reaction of, with fluorescein isothiocyanate-serum albumin conjugates, for hormone receptor detection)

IT 51505-54-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and reaction of, with fluoroscein isothiocyanate-serum albumin conjugates, for progesterone receptor detection)

IT 27072-45-3DP, reaction products with serum albumin  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and reaction of, with steroid hormone derivs., for hormone receptors detection)

IT 24516-38-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and reaction of, with thioglycolic acid)

IT 43188-86-9DP, reaction products with fluoroscein isothiocyanate-serum albumin conjugate  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, for cortisol receptor detection)

IT 40844-99-3DP, reaction products with fluorescein isothiocyanate-serum albumin conjugate 63235-88-1DP, reaction products with fluorescein isothiocyanate-serum albumin conjugate  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of, for testosterone receptor detection)

IT 2921-14-4  
RL: RCT (Reactant)  
(reaction of, with oxoestradiol)

IT 50-27-1 57-91-0 145-13-1 26445-07-8 27178-64-9 53-16-7,  
biological studies

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RL: ANST (Analytical study)  
    (receptors for, fluorescent cytochem. detection of, in neoplasms)  
IT 50-28-2, biological studies 57-83-0, biological studies  
RL: BIOL (Biological study)  
    (receptors for, for fluorescent cytochem. detection of, in neoplasms)

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L15 24 SEA FILE=REGISTRY ABB=ON PLU=ON (AZIDE/CN OR "AZIDE (H(N3)21-)" /CN OR "AZIDE (H(N3)21-), TETRAPHENYLPHOSPHONIUM"/CN OR "AZIDE (N3-)" /CN OR "AZIDE DIBENZYLDMETHYLAMMONIUM"/CN OR "AZIDE ION"/CN OR "AZIDE ION(1-)" /CN OR "AZIDE RADICAL"/CN OR "AZIDE(1-)" /CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3-OOXOCTADECAOXOCTADECAVANADATE(10-) (1:1)" /CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3-OOXOCTADECAOXOCTADECAVANADATE(13-) (1:1)" /CN OR "AZIDE, LABELED WITH NITROGEN-15"/CN OR "AZIDE, MONOHYDRATE"/CN OR AZIDE-1-15N/CN OR AZIDE-15N2/CN OR AZIDE-15N3/CN OR AZIDE-2-15N/CN OR AZIDIAMANTANE/CN OR "AZIDIC ACID"/CN OR AZIDIN/CN OR AZIDIN-NAGANIN/CN OR AZIDINE/CN OR "AZIDINE FAST SCARLET 4BS"/CN OR "AZIDINE FAST SCARLET 7BS"/CN OR "AZIDINE FAST SCARLET GGS"/CN OR "AZIDINE YELLOW 5G"/CN OR AZIDIOL/CN OR AZIDITHION/CN OR AZIDO/CN OR "AZIDO RADICAL"/CN)

L16 16 SEA FILE=REGISTRY ABB=ON PLU=ON "AZIDE" AND L15

L18 545 SEA FILE=REGISTRY ABB=ON PLU=ON "AZID"

L19 3867 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

L20 36392 SEA FILE=HCAPLUS ABB=ON PLU=ON L18

L21 141428 SEA FILE=HCAPLUS ABB=ON PLU=ON (N3 OR ?AZID? OR NITRENE OR SINGLET OXYGEN)

L22 2611 SEA FILE=HCAPLUS ABB=ON PLU=ON DYE(L) (L19 OR L20 OR L21)

L23 191092 SEA FILE=HCAPLUS ABB=ON PLU=ON ?CYANIN? OR ?RHODAMIN? OR ?PHENOXAZIN? OR ?PHENOTHIZIN? OR ?PHENOSELENAZIN? OR ?FLUORESCIN? OR ?PORPHYRIN? OR ?BENZOPORPHYRIN? OR ?SQUARAIN? OR ?CORRIN? OR ?COROCONIUM? OR AZO(W)DYE OR METHIN?(W)DYE OR INDOLENIUM(W)DYE

L24 586 SEA FILE=HCAPLUS ABB=ON PLU=ON L22(L)L23

L27 13956 SEA FILE=HCAPLUS ABB=ON PLU=ON RECEPTOR(5A) (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)

L29 163257 SEA FILE=HCAPLUS ABB=ON PLU=ON (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)

L30 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L24

L31 90 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L23

L32 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 AND L31

L33 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 OR L32

L34 88 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L21

L35 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L34 AND L23

L38 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L29

L39 53 SEA FILE=HCAPLUS ABB=ON PLU=ON L27(L)L23

L40 55 SEA FILE=HCAPLUS ABB=ON PLU=ON (L19 OR L20 OR L21) (L)L27

L44 318 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPOCRELLIN?

L45 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L44

L46 65735 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPOCRELLIN? OR AZO OR METHINE OR INDOLENIUM

L47 429 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L46

L48 429 SEA FILE=HCAPLUS ABB=ON PLU=ON L47 AND DYE

L50 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L48 AND L29

L57 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L39 AND PATENT/DT

L58 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L57 AND PRD<20010307

L59 44 SEA FILE=HCAPLUS ABB=ON PLU=ON L39 NOT L57

L60 43 SEA FILE=HCAPLUS ABB=ON PLU=ON L59 AND PD<20010307

L61 52 SEA FILE=HCAPLUS ABB=ON PLU=ON L58 OR L60

L62 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L40(L)CONJUGAT?

L63 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L40 AND CONJUGAT?

L64 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L40 AND (COVALENT? OR BOND? OR LINK?)



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L65 27 SEA FILE=HCAPLUS ABB=ON PLU=ON (L62 OR L63 OR L64)  
L66 3966 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 AND (L23 OR L46)  
L67 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L66 AND L29  
L68 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L67 NOT (L65 OR L61 OR L50 OR  
L45 OR (L32 OR L33) OR L38 OR L35)  
L69 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L68 AND (CONJUGAT? OR  
RECEPTOR)  
L70 19 SEA FILE=HCAPLUS ABB=ON PLU=ON L68 NOT L69

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L70 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:838129 HCAPLUS

DOCUMENT NUMBER: 134:5118

TITLE: Derivatized oligonucleotides having improved uptake and other properties

INVENTOR(S): Manoharan, Muthiah; Cook, Phillip Dan; Bennett, Clarence Frank

PATENT ASSIGNEE(S): ISIS Pharmaceuticals, Inc., USA

SOURCE: U.S., 25 pp., Cont.-in-part of U.S. Ser. No. 782,374, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 92

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6153737	A	20001128	US 1994-211882	19940422
WO 9110671	A1	19910725	WO 1991-US243	19910111
W: AU, BR, CA, FI, HU, JP, KR, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2089376	AA	19920214	CA 1991-2089376	19910812
WO 9307883	A1	19930429	WO 1992-US9196	19921023
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 5578718	A	19961126	US 1993-116801	19930903
JP 08098700	A2	19960416	JP 1995-175173	19950711
AU 713740	B2	19991209	AU 1997-26244	19970624
AU 9726244	A1	19971106		
US 6232463	B1	20010515	US 1998-128508	19980804
US 6265558	B1	20010724	US 1999-383856	19990826
PRIORITY APPLN. INFO.:			US 1990-463358	B2 19900111
			US 1990-566977	B2 19900813
			WO 1991-US243	A2 19910111
			US 1991-782374	B2 19911024
			WO 1992-US9196	W 19921023
			AU 1993-38025	A3 19930225
			US 1993-116801	A2 19930903
			US 1994-211882	A2 19940422
			US 1995-458396	A1 19950602
			US 1997-924326	A1 19970905
			US 1997-948151	A1 19971009

AB Linked nucleosides having at least one functionalized nucleoside that bears a substituent such as a **steroid** mol., a reporter mol., a non-arom. lipophilic mol., a reporter enzyme, a peptide, a protein, a water sol. vitamin, a lipid sol. vitamin, an RNA cleaving complex, a metal chelator, a **porphyrin**, an alkylator, a pyrene, a hybrid photo-nuclease/intercalator, or an aryl **azide** photo-crosslinking agent exhibit increased cellular uptake and other properties. The substituent can be attached at the 2'-position of the functionalized nucleoside via a linking group. If at least a portion of the remaining linked nucleosides are 2'-deoxy-2'-fluoro, 2'-O-methoxy, 2'-O-ethoxy, 2'-O-propoxy, 2'-O-aminoalkoxy or 2'-O-allyloxy nucleosides, the substituent can be attached via a linking group at any of the 3' or the 5' positions of the nucleoside or on the heterocyclic base of the nucleoside

or on the inter-nucleotide linkage linking the nucleoside to an adjacent nucleoside.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:738842 HCAPLUS

DOCUMENT NUMBER: 133:301194

TITLE: Medical device-bound gelatin hydrogels loaded with liposomes for drug

INVENTOR(S): Dicosmo, Frank; Ditizio, Valerio

PATENT ASSIGNEE(S): Uroteq Inc., Can.

SOURCE: U.S., 16 pp., Cont.-in-part of U. S. Ser. No. 631,326, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6132765	A	20001017	US 1997-843342	19970415
WO 9846287	A2	19981022	WO 1998-CA351	19980415
WO 9846287	A3	19990211		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9870198	A1	19981111	AU 1998-70198	19980415
AU 736584	B2	20010802		
EP 984798	A2	20000315	EP 1998-916701	19980415
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
JP 2001523124	T2	20011120	JP 1998-543334	19980415
US 6228393	B1	20010508	US 1999-412584	19991005
US 2002009485	A1	20020124	US 2001-818649	20010328
US 2002051812	A1	20020502	US 2001-849481	20010507
PRIORITY APPLN. INFO.:			US 1996-631326	B2 19960412
			US 1997-843342	A2 19970415
			WO 1998-CA351	W 19980415
			US 1999-412584	A1 19991005

AB The present invention is directed to a vehicle for affecting drug delivery from a solid substrate. Hydrogels loaded with liposomal therapeutic agents such as antibiotics are covalently bonded to the surface of substrates such as in-dwelling medical devices, implants, catheters, and the like. The present invention is particularly useful in the treatment and prevention of biofilm mediated infection often assocd. with the use of in-dwelling medical devices. For example, a silicone catheters were coated with PEG-crosslinked gelatin hydrogel loaded with liposome-encapsulated ciprofloxacin for prevention of bacterial infections.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L70 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:259972 HCAPLUS  
 DOCUMENT NUMBER: 132:293042  
 TITLE: Encapsulation of sensitive liquid components into a matrix to obtain discrete shelf-stable particles  
 INVENTOR(S): Van Lengerich, Bernhard H.  
 PATENT ASSIGNEE(S): General Mills, Inc., USA  
 SOURCE: PCT Int. Appl., 56 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021504	A1	20000420	WO 1999-US20905	19991006
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9963872	A1	20000501	AU 1999-63872	19991006
EP 1119345	A1	20010801	EP 1999-951433	19991006
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2000004784	A	20000925	NO 2000-4784	20000925
PRIORITY APPLN. INFO.: US 1998-103700P P 19981009 US 1998-109696P P 19981124 US 1999-233443 A 19990120 US 1998-79060P P 19980323 WO 1999-US4267 W 19990323 WO 1999-US20905 W 19991006				
AB A liq. encapsulant component which contains an active, sensitive encapsulant, such as a live microorganism or an enzyme dissolved or dispersed in a liq. plasticizer is admixed with a plasticizable matrix material. The matrix material is plasticizable by the liq. plasticizer and the encapsulation of the active encapsulant is accomplished at a low temp. and under low shear conditions. The active component is encapsulated and/or embedded in the plasticizable matrix component or material in a continuous process to produce discrete, solid particles. The liq. content of the liq. encapsulant component provides substantially all or completely all of the liq. plasticizer needed to plasticize the matrix component to obtain a formable, extrudable, cuttable, mixt. or dough. Removal of liq. plasticizer prior to extrusion is not needed to adjust the viscosity of the mixt. for formability. Release of an active component from the matrix may be delayed or controlled over time so that the active component is delivered when and where it is needed to perform its intended function. Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant.				
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L70 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:542564 HCAPLUS  
 TITLE: Synthesis and photophysics of new types of fullerene-**porphyrin** dyads.  
 AUTHOR(S): Schuster, David I.  
 CORPORATE SOURCE: Chemistry Department, New York University, New York, NY, 10003, USA  
 SOURCE: Book of Abstracts, 218th ACS National Meeting, New Orleans, Aug. 22-26 (1999), ORGN-185. American Chemical Society: Washington, D. C.  
 CODEN: 67ZJA5  
 DOCUMENT TYPE: Conference; Meeting Abstract  
 LANGUAGE: English

AB There is considerable interest currently in compounds in which C60, a powerful electron acceptor, is covalently linked to electron donors. Such compounds are model systems for studies of photoinduced intramolecular electron transfer and energy transfer processes, and have potential applications in biology. We have conducted in recent years on the synthesis of a variety of **porphyrin**-C60 dyads with both flexible (e.g., polyether) and rigid (**steroid**) linkers, and on bridged 'parachute-shaped' dyads in which the **porphyrin** and C60 moieties are in very close proximity. Methods for synthesis of all three types of dyads will be presented. We have studied quenching of the **porphyrin** fluorescence as a function of the mode of linkage of the **porphyrin** and the fullerene, and have measured fluorescence lifetimes and quantum efficiencies of sensitized **singlet oxygen** formation in all cases. Comparison of data in nonpolar and polar solvents provides insight into the dynamic competition between intramolecular electron transfer and energy transfer processes in these dyads.

L70 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:518285 HCAPLUS  
 DOCUMENT NUMBER: 131:144789  
 TITLE: Preparation of steroidal glycosides as hypocholesterolemic and antiatherosclerosis agents  
 INVENTOR(S): Deninno, Michael Paul  
 PATENT ASSIGNEE(S): Pfizer Inc., USA  
 SOURCE: U.S., 34 pp., Cont. of U.S. Ser. No. 652,478.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5939398	A	19990817	US 1998-9037	19980120
PRIORITY APPLN. INFO.:			US 1996-652478	19960618
OTHER SOURCE(S):	MARPAT 131:144789			
GI				

AB This invention relates to certain steroidal glycosides useful as hypocholesterolemic agents and antiatherosclerosis agents and certain protected intermediates useful in the prepn. of said steroidal glycosides. The title compds. [I; X = CO, (R)- or (S)-CH(OH); Y = CO, CH<sub>2</sub>, (R)- or (S)-CH(OH); R<sub>1</sub> - R<sub>3</sub> = H, OH, halo, NH<sub>2</sub>, **N3**, C<sub>1</sub>-6 alkoxy-C<sub>1</sub>-6 alkoxy, Z-R<sub>4</sub>; wherein Z = NHCO, O<sub>2</sub>C, CO<sub>2</sub>, NR<sub>5</sub>, NHCONR<sub>5</sub>, OCSNR<sub>5</sub>; R<sub>4</sub> = each (un)substituted aryl, aryl-C<sub>1</sub>-6 alkyl, C<sub>2</sub>-4 alkenyl, C<sub>1</sub>-6 alkyl, C<sub>3</sub>-7 cycloalkyl, or C<sub>3</sub>-7 cycloalkyl-C<sub>1</sub>-6 alkyl; wherein R<sub>5</sub> = H, C<sub>1</sub>-4 alkyl; NR<sub>5</sub> and R<sub>4</sub> which is a covalent bond are taken together to form pyrrolidinyl, piperidinyl, N-methylpiperazinyl, indolinyl, or morpholinyl each optionally substituted on the C atom with C<sub>1</sub>-4 alkoxy-carbonyl], useful for the treatment of hypercholesterolemia and atherosclerosis, are prep'd. Thus, (3.β., 5.α., 25R)-3-[[4'-(2-fluorophenyl)carbonyl]-.β.-D-cellobiosyl]oxy]spirostan-11-one was prep'd. for the treatment of hypercholesterolemia and atherosclerosis. However, an effective dosage is in the range of 0.005 to 20 mg/kg/day, preferably 0.01 to 5 mg/kg/day, most preferably 0.01 to 1 mg/kg/day. For an av. 70 kg human, this would amt. to 0.00035 to 1.4 g/day, preferably 0.0007 to 0.35 g/day, most preferably 0.0007 to 0.07 g/day. In one mode of administration the compds. of this invention are taken with meals.

L70 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1998:526684 HCAPLUS  
TITLE: Photophysical properties of new types of fullerene-  
**porphyrin** hybrids.  
AUTHOR(S): Schuster, David I.; Baran, Philip S.; Fong, Robert,  
II; Cheng, Peng  
CORPORATE SOURCE: Department Chemistry, New York University, New York,  
NY, 10003, USA  
SOURCE: Book of Abstracts, 216th ACS National Meeting, Boston,  
August 23-27 (1998), PHYS-245. American Chemical  
Society: Washington, D. C.  
CODEN: 66KYA2  
DOCUMENT TYPE: Conference; Meeting Abstract  
LANGUAGE: English  
AB Routes for synthesis of hybrid mols. in which buckminsterfullerene, C60,  
is coupled to **tetraphenylporphyrin** with a variety of flexible  
polyether linkages as well as acetylenic, arom. and **steroid**

linkers, have recently been developed in our lab. The extent to which these two chromophoric moieties interact intramolecularly in ground and excited states has been detd. using UV-VIS absorption and fluorescence spectroscopy, electrochem., <sup>3</sup>He NMR and quantum yields for sensitized formation of **singlet oxygen**. The exptl. results confirm mol. modeling computation which indicate that conformations are adopted which bring the two chromophores close together in space. Studies on the first C60-**porphyrin** cyclophanes will also be presented.

L70 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:293427 HCAPLUS  
 DOCUMENT NUMBER: 129:8597  
 TITLE: Embedding and encapsulation of controlled release particles  
 INVENTOR(S): Van Lengerich, Bernhard H.  
 PATENT ASSIGNEE(S): Van Lengerich, Bernhard H., USA  
 SOURCE: PCT Int. Appl., 63 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818610	A1	19980507	WO 1997-US18984	19971027
W: AU, CA, JP, NO, PL, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9749915	A1	19980522	AU 1997-49915	19971027
EP 935523	A1	19990818	EP 1997-912825	19971027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002511777	T2	20020416	JP 1998-520558	19971027
NO 9902036	A	19990428	NO 1999-2036	19990428
PRIORITY APPLN. INFO.:			US 1996-29038P	P 19961028
			US 1997-52717P	P 19970716
			WO 1997-US18984	W 19971027

AB Controlled release, discrete, solid particles which contain an encapsulated and/or embedded component such as a heat sensitive or readily oxidizable pharmaceutically, biol., or nutritionally active component are continuously produced without substantial destruction of the matrix material or encapsulant. A release-rate controlling component is incorporated into the matrix to control the rate of release of the encapsulant from the particles. The addnl. component may be a hydrophobic component or a high water binding capacity component for extending the release time. The plasticizable matrix material, such as starch, is admixed with at least one plasticizer, such as water, and at least one release-rate controlling component under low shear mixing conditions to plasticize the plasticizable material without substantially destroying the at least one plasticizable material and to obtain a substantially homogeneous plasticized mass. The plasticizer content is substantially reduced and the temp. of the plasticized mass is substantially reduced prior to admixing the plasticized mass with the encapsulant to avoid substantial destruction of the encapsulant and to obtain a formable, extrudable mixt. The mixt. is extruded through a die without substantial or essentially no expansion and cut into discrete, relatively dense particles. Release properties may also be controlled by precoating the encapsulant and/or coating the extruded particles with a film-forming component. An example of encapsulation of acetylcysteine is given using starch, polyethylene, glycerol monostearate, and vegetable oil.

L70 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:207280 HCAPLUS

DOCUMENT NUMBER: 128:275101

TITLE: Gas and gaseous precursor filled microspheres as topical and subcutaneous delivery vehicles

INVENTOR(S): Unger, Evan C.; Matsunaga, Terry O.; Yellowhair, David

PATENT ASSIGNEE(S): Imarx Pharmaceutical Corp., USA

SOURCE: U.S., 40 pp. Cont.-in-part of U.S. Ser. No. 307,305.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 19

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5733572	A	19980331	US 1994-346426	19941129
US 5088499	A	19920218	US 1990-569828	19900820
WO 9109629	A1	19910711	WO 1990-US7500	19901219
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
JP 05502675	T2	19930513	JP 1991-503276	19901219
AT 180170	E	19990615	AT 1991-902857	19901219
ES 2131051	T3	19990716	ES 1991-902857	19901219
US 5228446	A	19930720	US 1991-717084	19910618
WO 9222247	A1	19921223	WO 1992-US2615	19920331
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
AU 9220020	A1	19930112	AU 1992-20020	19920331
AU 667471	B2	19960328		
JP 06508364	T2	19940922	JP 1992-500847	19920331
EP 616508	A1	19940928	EP 1992-912456	19920331
EP 616508	B1	20010718		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
AT 203148	E	20010815	AT 1992-912456	19920331
ES 2159280	T3	20011001	ES 1992-912456	19920331
US 5469854	A	19951128	US 1993-76239	19930611
US 5580575	A	19961203	US 1993-76250	19930611
US 5348016	A	19940920	US 1993-88268	19930707
US 5542935	A	19960806	US 1993-160232	19931130
US 5585112	A	19961217	US 1993-159687	19931130
US 5769080	A	19980623	US 1994-199462	19940222
WO 9428874	A1	19941222	WO 1994-US5633	19940519
W: AU, CA, CN, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5773024	A	19980630	US 1994-307305	19940916
CA 2177713	AA	19950608	CA 1994-2177713	19941130
JP 09506098	T2	19970617	JP 1994-515763	19941130
US 5571497	A	19961105	US 1995-468056	19950606
CN 1180310	A	19980429	CN 1996-193069	19960327
US 6001335	A	19991214	US 1996-665719	19960618
US 5935553	A	19990810	US 1996-758179	19961125
US 5985246	A	19991116	US 1997-888426	19970708
AU 713127	B2	19991125	AU 1998-56271	19980224
AU 9856271	A1	19980507		
AU 9888405	A1	19981203	AU 1998-88405	19981012
AU 731072	B2	20010322		
AU 9910043	A1	19990304	AU 1999-10043	19990104
PRIORITY APPLN. INFO.:			US 1989-455707	B2 19891222



US 1990-569828	A2 19900820
US 1991-716899	B2 19910618
US 1991-717084	A2 19910618
US 1993-76239	A2 19930611
US 1993-76250	A2 19930611
US 1993-159674	B2 19931130
US 1993-159687	A2 19931130
US 1993-160232	A2 19931130
US 1994-307305	A2 19940916
WO 1990-US7500	W 19901219
US 1991-750877	A3 19910826
US 1992-818069	A3 19920108
WO 1992-US2615	A 19920331
US 1992-967974	A3 19921027
US 1993-17683	A3 19930212
US 1993-18112	B3 19930217
US 1993-85608	A3 19930630
US 1993-88268	A3 19930707
US 1993-163039	A3 19931206
US 1994-212553	B2 19940311
AU 1994-70416	A3 19940519
US 1994-346426	19941129
AU 1995-21850	A3 19941130
WO 1994-US13817	W 19941130
US 1995-395683	A3 19950228
US 1995-468056	A3 19950606
US 1995-471250	A3 19950606
US 1996-665719	A3 19960618

AB Gas and gaseous precursor filled microspheres, and foams provide novel topical and s.c. delivery vehicles for various active ingredients, including drugs and cosmetics. Gas and gaseous precursor filled microcapsules were prepd. from dipalmitoylphosphatidylcholine.

L70 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:403686 HCAPLUS

DOCUMENT NUMBER: 119:3686

TITLE: Substrate specificities of two stably expressed human liver UDP-glucuronosyltransferases of the UGT1 gene family

AUTHOR(S): Ebner, Thomas; Burchell, Brian

CORPORATE SOURCE: Dep. Biochem. Med., Univ. Dundee, Dundee, DD1 9SY, UK

SOURCE: Drug Metab. Dispos. (1993), 21(1), 50-5

CODEN: DMDSAI; ISSN: 0090-9556

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two cloned human hepatic UDP-glucuronosyltransferase (UGT) cDNAs were stably expressed in Chinese hamster V79 cells. More than 100 drugs and xenobiotics were used as substrates for glucuronidation catalyzed by the cloned human UGT isoenzymes to det. the chem. structures accepted as substrates. UGT HP1 exhibited a limited substrate specificity for planar phenolic compds., whereas UGT HP4 was more promiscuous in acceptance of nonplanar phenols, anthraquinones, flavones, aliph. alcs., arom. carboxylic acids, **steroids**, and many drugs of varied structure. Levels of HP4 UGT activity toward some substrates were sufficient to allow detn. of kinetic parameters for the enzyme reaction. The metab. of drugs could be studied by addn. to the recombinant cell lines in culture, and extn. of the media allowed anal. of glucuronide formation. The data presented here demonstrate the potential of using these recombinant cell lines for investigation of phase II metab. by human UGTs.

L70 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1988:488917 HCAPLUS

DOCUMENT NUMBER: 109:88917

TITLE: Protection against **dihematoporphyrin** ether  
photosensitivityAUTHOR(S): Manyak, Michael J.; Smith, Paul D.; Harrington, Frank  
S.; Steinberg, Seth M.; Glatstein, Eli; Russo, Angelo

CORPORATE SOURCE: Radiat. Oncol. Branch, NIH, Bethesda, MD, 20892, USA

SOURCE: Photochem. Photobiol. (1988), 47(6), 823-30

CODEN: PHCBAP; ISSN: 0031-8655

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Amelioration of **dihematoporphyrin** ether (DHE)-induced skin photosensitivity by medications either suspected or known to influence **porphyrin** metab. or inflammatory response was evaluated in female athymic NCR-nude mice (308 study animals, 49 controls) in 56 sep. study groups. At 72 h after injection with 25 mg/kg of DHE, the study animals' abdomens were irradiated with 4.125-4.25 J/cm<sup>2</sup> of visible light. Controls were irradiated after receiving either medication, solubilizing agent, or no injection. The abdominal surface burns were examd. daily and graded as extensive, partial, or no burn. Statistical comparison was made between irradiated mice injected with DHE only and irradiated mice injected with DHE and medication. Injection of medications which influenced metab. (hydroxychloroquine, **hydrochlorothiazide**) produced fewer extensive but greater frequencies of partial burns than DHE controls. Medications which block histamine effect (cimetidine and/or hydroxyzine) resulted in fewer extensive and roughly equal frequencies of partial burns compared with DHE controls. **Steroids** (dexamethasone, methylprednisolone, triamcinolone) with interfere with inflammatory response resulted in similar extensive and partial burn levels. Control animals receiving only medication, solubilizing agent, or no injection had no photosensitivity and consequently showed no burns. The results from this study suggest that inhibition of histamine effect and, to a lesser extent, increased activity of **porphyrin** catabolic pathways may decrease skin photosensitivity assocd. with DHE administration.

L70 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1982:490273 HCAPLUS

DOCUMENT NUMBER: 97:90273

TITLE: From crosslinking to capping: order of intermediate  
events

AUTHOR(S): Ashman, Robert F.; Karlan, Beth Young

CORPORATE SOURCE: Sch. Med., Univ. California Los Angeles, Los Angeles,  
CA, USASOURCE: Dev. Immunol. (1981), 15(B Lymphocytes Immune  
Response: Funct., Dev., Interact. Prop.), 163-7

CODEN: DEIMD6; ISSN: 0163-5921

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The capping of surface Ig on CBA/J mouse spleen B lymphocytes was obsd. by exposing the cells (with or without the inhibitors present) at 4.degree. for 20 min to polyspecific goat anti-mouse Ig (labeled with **fluorescein**); cells were scored for capping by fluorescence microscopy. The degree of inhibition and reversibility were scored; inhibition in the forward direction averaged 70%; inhibition in the reverse direction averaged 15%. The inhibited steps form the following unique linear sequence: hydrocortisone .fwdarw. chlorpromazine and Ca ionophore A23187 in uncertain order .fwdarw. cytochalasins B and D .fwdarw. propranolol .fwdarw. dibucaine .fwdarw. F- .fwdarw. N3 -. Thus, the rapid capping response of the lymphocyte triggered by

surface Ig cross-linking provides an instructive example of a membrane-generated signal, whose component steps may be dissected by using reversible inhibitors. The exptl. detd. order of these steps suggests the following outline of the progress of the capping signal: crosslinked surface Ig makes contact with another membrane mol. in a manner sensitive to membrane fluidity changes (**steroid** site). This mol. participates in a Ca-dependent linkage to cytoplasmic contractile proteins (chlorpromazine site) which must interact with other proteins (ionophore A23187 site) before assembly into functional microfilaments (cytochalasin site). Then Ca translocations across internal membranes (propranolol and dibucaine sites) precede the energy-requiring contraction (F- and N3- sites, i.e. glycolysis and electron transport in the mitochondria, resp.).

L70 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1981:569582 HCAPLUS

DOCUMENT NUMBER: 95:169582

TITLE: Oxidation of ketone and aldehyde hydrazones, oximes and semicarbazones, and of hydroxylamines, and hydrazo-compounds, using benzeneseleninic anhydride  
 AUTHOR(S): Barton, Derek H. R.; Lester, David J.; Ley, Steven V.  
 CORPORATE SOURCE: Dep. Chem., Imp. Coll., London, SW7 2AY, Engl.  
 SOURCE: J. Chem. Soc., Perkin Trans. 1 (1980), (6), 1212-17  
 CODEN: JCPRB4; ISSN: 0300-922X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Treatment of arom., aliph., and steroidal hydrazones, oximes, and semicarbazones with (PhSeO)2O in THF at 50.degree. resulted in regeneration of the aldehyde or ketone. E.g., cholestanone phenylhydrazone, p-nitrophenylhydrazone, p-toluenesulfonylhydrazone, oxime, and semicarbazone gave 64, 95, 97, 83, and 83%, resp., cholestanone. PhCH:NNHPh with (PhSeO)2O gave 73% benzoylazobenzene. The ketoazo species were also prepd. by oxidn. of the corresponding **hydrazide** with (PhSeO)2O. Arom. and aliph. **hydrazides** and hydroxylamines were oxidized to **azo** and nitroso compds.

L70 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1980:191212 HCAPLUS

DOCUMENT NUMBER: 92:191212

TITLE: Effects of various pharmacologic agents on allergic inflammation of the eye. The roles of chemical mediators in ocular inflammation

AUTHOR(S): Okada, Mariko; Shimada, Kohkichi

CORPORATE SOURCE: Tokyo Metrop. Inst. Med. Sci., Tokyo, Japan

SOURCE: Invest. Ophthalmol. Visual Sci. (1980), 19(2), 176-81  
 CODEN: IOVSDA; ISSN: 0146-0404

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Effects of pharmacologic agents on exptl. ocular inflammation induced by reverse passive Arthus reactions were investigated by a slit-lamp technique utilizing **fluorescein**-labeled rabbit serum albumin as an indicator. Cobra venom factor completely eliminated inflammatory responses, indicating that the complement system is a trigger for this type of ocular inflammation. Antihistamines mainly suppressed the early vascular response. Reserpine [50-55-5] and indomethacin [53-86-1] remarkably inhibited the increase of the permeability of the blood-aq. barrier over the first 5 h. Epinephrine [51-43-4] and **steroid** hormone were also effective. Neither diethylcarbamazine [90-89-1] nor isonicotinic acid **hydrazide** [54-85-3] showed effects on the permeability changes induced in this type of inflammation.

L70 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1977:43894 HCAPLUS

DOCUMENT NUMBER: 86:43894

TITLE: Reactions with organophosphorus compounds. XLI. New synthetic aspects of the triphenylphosphine-diethyl azodicarboxylate-hydroxy compound system

AUTHOR(S): Loibner, Hans; Zbiral, Erich

CORPORATE SOURCE: Org.-Chem. Inst., Univ. Wien, Vienna, Austria

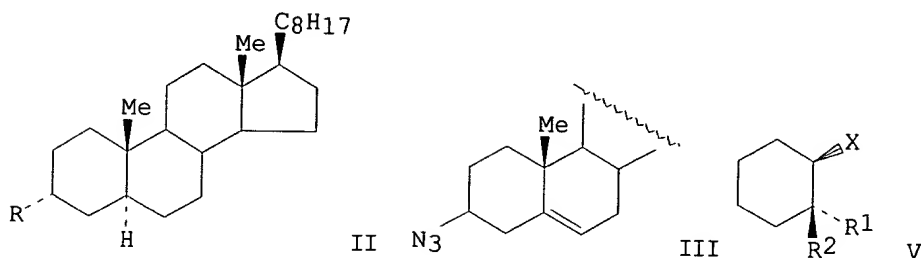
SOURCE: Helv. Chim. Acta (1976), 59(6), 2100-13

CODEN: HCACAV

DOCUMENT TYPE: Journal

LANGUAGE: German

GI



AB Reaction of hydroxy compds. with nucleophiles in the  $\text{Ph}_3\text{P-EtO}_2\text{CN:NCO}_2\text{Et}$  (I) system was studied. Thus, cholestanes II ( $\text{R} = \text{N}_3, \text{CN}, \text{SCN}, \text{O}_2\text{CCF}_3, \text{SPh}$ ) were prepd. in 25-96% yields from 5.alpha.-cholestan-3.beta.-ol. Cholesterol was converted to III on treatment with  $\text{HN}_3$  without any neighboring group participation by the C-5 double bond. The reaction of vitamin D<sub>3</sub> (IV) with 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>H in the presence of the I system gave 50% 3-epivitamin D<sub>3</sub> 4-nitrobenzoate, whereas using 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>COCl and pyridine the 4-nitrobenzoate of IV was obtained. Also prepd. were I ( $\text{R} = \text{Br}, \text{Cl}, \text{I}, \text{O}_3\text{SOMe}, \text{O}_3\text{SC}_6\text{H}_4\text{Me-4}$ ) in 50-90% yields from 5.alpha.-cholestan-3.beta.-ol and RR<sub>1</sub> ( $\text{R}_1 = \text{Me}$ ) using the I system. The tosylation of (S)-2-butanol using the above system gave (R)-2-butyl tosylate. Cis-cyclohexanes I ( $\text{X} = \text{N}_3, \text{Cl}; \text{R}_1 = \text{H}, \text{R}_2 = \text{N}_3, \text{I}$ ) were obtained from the trans-cyclohexanols V ( $\text{X} = \text{N}_3, \text{Cl}; \text{R}_1 = \text{OH}, \text{R}_2 = \text{H}$ ) using MeI and  $\text{HN}_3$ .

L70 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1975:497714 HCAPLUS

DOCUMENT NUMBER: 83:97714

TITLE: Rose Bengal sensitized type-II photooxygenation (singlet oxygen reaction) of

3.beta.-acetoxy-.DELTA.7-cholestene and

3.beta.,7.alpha.-diacetoxy-.DELTA.8(14)-cholestene

AUTHOR(S): Schenck, Guenther O.; Eisfeld, Wolfgang; Neumueller, Otto A.

CORPORATE SOURCE: Inst. Strahlenchem., Max-Planck-Inst. Kohlenforsch., Muelheim, Ger.

SOURCE: Justus Liebig's Ann. Chem. (1975), (4), 701-11

CODEN: JLACBF

DOCUMENT TYPE: Journal

LANGUAGE: German

GI For diagram(s), see printed CA Issue.  
 AB Photooxidn. of 3.beta.-acetoxy-5.alpha.-cholest-7-ene in presence of rose bengal or **hematoporphyrin** gave hydroperoxides I and II via III. 3.beta.,7.alpha.-Diacetoxy-5.alpha.-cholest-8(14)-ene reacted similarly.

L70 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1973:84644 HCAPLUS

DOCUMENT NUMBER: 78:84644

TITLE: Chemical evidence of transition-state geometry in reaction of monoolefins with **singlet oxygen**

AUTHOR(S): Nickon, Alex; DiGiorgio, Joseph B.; Daniels, Peter J. L.

CORPORATE SOURCE: Dep. Chem., Johns Hopkins Univ., Baltimore, Md., USA

SOURCE: J. Org. Chem. (1973), 38(3), 533-9

CODEN: JOCEAH

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To examine the possibility of stereoelectronic control in formation of the C-O bond in oxygenation of monoolefins with singlet O, steroidal substrates were studied having allylic Me groups in which optimum C-H orientation for a cyclic process is readily attainable. **Hematoporphyrin**-sensitized oxygenation of 3-methyl-5.alpha.-cholest-2-ene in pyridine followed by redn. of the initially formed hydroperoxides afforded 7:3 3.beta.-methyl-5.alpha.-cholest-1-en-3.alpha.-ol -3-methylene-5.alpha.-cholestan-2.alpha.-ol. Under similar conditions, 2-methyl-5.alpha.-cholest-2-ene gave 57:13:30 2-methylene-5.alpha.-cholestan-3.alpha.-ol -2-methylene-5.alpha.-cholestan-3.beta.-ol -2-methyl-5.alpha.-cholest-1-en-3.alpha.-ol. Formation of a quasi-axial C-O bond may be slightly favored over a quasi-equatorial one, but the preference is not as strong as that obsd. for cleavage of a quasi-axial C-H bond over a quasi-equatorial C-H in endocyclic cyclohexene systems. A transition state for the cyclic, product-forming step that resembles starting olefin more than it does the allylic hydro-peroxide product accounts for these results.

L70 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1973:72436 HCAPLUS

DOCUMENT NUMBER: 78:72436

TITLE: .DELTA.6-Estrenes

INVENTOR(S): Van Vliet, Nicolaas Pieter; Peters, Jacobus A. M.

PATENT ASSIGNEE(S): Organon Inc.

SOURCE: U.S., 5 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 3708511	A	19730102	US 1972-218837	19720118
GI	For diagram(s), see printed CA Issue.				
AB	Activated O, prepd. by irradiation of O in the presence of <b>hematoporphyrin</b> or decomposition of the ozonide of P(OPh) <sub>3</sub> , converted the estrenes I (R = H, Ac) to the corresponding hydroperoxides II (R <sub>1</sub> = OOH). The latter were treated with NaHSO <sub>3</sub> to yield II (R = H, Ac; R <sub>1</sub> = OH), which possessed ovulation-inhibiting and estrogenic activity. Similarly, estr-5-en-17-one gave 5.alpha.-hydroxyestr-6-en-17-one.				

L70 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1968:403069 HCAPLUS

DOCUMENT NUMBER: 69:3069

TITLE: Nitrogen-containing **steroids**. XX. Addition of **chlorazide** and **bromazide** to 3-oxo-.DELTA.4-**steroids**

AUTHOR(S): Drefahl, Guenther; Ponsold, Kurt; Eichhorn, Dieter

CORPORATE SOURCE: Univ. Jena, Jena, Ger.

SOURCE: Chem. Ber. (1968), 101(5), 1633-42

CODEN: CHBEAM

DOCUMENT TYPE: Journal

LANGUAGE: German

AB Following the addn. of **haloazides** to 3-oxo-.DELTA.4-**steroids**, such as testosterone propionate and progesterone, the halogen entered in position 4 and the **azido** group in 5. Progesterone gave a homogeneous addn. product, while testosterone propionate or testosterone acetate gave 2 isomers. The configuration of the isomers was elucidated by redn.

L70 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1949:46619 HCAPLUS

DOCUMENT NUMBER: 43:46619

ORIGINAL REFERENCE NO.: 43:8421c-e

TITLE: A new reagent for the histochemical demonstration of active carbonyl groups. A new method for staining ketonic **steroids**

AUTHOR(S): Ashbel, Rivka; Seligman, Arnold M.

SOURCE: Endocrinology (1949), 44, 565-83

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

AB A new method for demonstrating carbonyl groups in the lipoid of HCHO-fixed tissues is described. It is based on the reaction of aldehyde and ketone groups with 2-hydroxy-3-naphthoic acid **hydrazide** followed by coupling of tetrazotized di-o-anisidine into the naphtholic ring with the production of a blue insol. **azo** compd. Reaction with certain carbonyl groups of nonlipoid material in nervous tissue, elastic tissue, and reticulum is also described. Carbonyl-reacting lipoid was found in adrenal cortex, corpus luteum, interstitial cells of testis, and syncytium of placenta. The localization in tissue was similar to that demonstrated by other methods. Evidence is presented that the carbonyl-reacting lipoid in these HCHO-fixed tissues is in fact ketosteroid.

L56 combines Hypocrellin, methine or azo dye

CEPERLEY 09/898,885

w/ conjugation to

=> d que 156

L1 345 SEA FILE=HCAPLUS ABB=ON PLU=ON RAJAGOPALAN R?/AU azide or singlet  
L2 49 SEA FILE=HCAPLUS ABB=ON PLU=ON BUGAJ J?/AU oxygen  
L3 48 SEA FILE=HCAPLUS ABB=ON PLU=ON DORSHOW R?/AU  
L4 44 SEA FILE=HCAPLUS ABB=ON PLU=ON ACHILEFU S?/AU  
L5 415 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4)  
L8 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L5 AND PHOTO?  
L9 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 AND DYE?  
L12 64 SEA FILE=REGISTRY ABB=ON PLU=ON (302794-43-0/BI OR 83150-76-9  
/BI OR 105466-87-3/BI OR 195825-84-4/BI OR 25679-24-7/BI OR  
309916-88-9/BI OR 309916-89-0/BI OR 309916-90-3/BI OR 115239-21  
-9/BI OR 31362-50-2/BI OR 351439-57-1/BI OR 41532-84-7/BI OR  
4224-70-8/BI OR 590-92-1/BI OR 67-68-5/BI OR 95781-56-9/BI OR  
95837-47-1/BI OR 141-43-5/BI OR 1640-39-7/BI OR 2531-70-6/BI  
OR 309916-92-5/BI OR 351439-58-2/BI OR 351439-59-3/BI OR  
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OR 204317-00-0/BI OR 204317-01-1/BI OR 204317-02-2/BI OR  
204317-03-3/BI OR 25126-32-3/BI OR 2785-06-0/BI OR 309916-91-4/  
BI OR 317809-26-0/BI OR 317809-27-1/BI OR 37221-79-7/BI OR  
401819-24-7/BI OR 401819-25-8/BI OR 411241-10-6/BI OR 411241-11  
-7/BI OR 411241-12-8/BI OR 411241-13-9/BI OR 411241-14-0/BI OR  
411241-15-1/BI OR 411241-16-2/BI OR 411241-17-3/BI OR 411241-18  
-4/BI OR 411241-19-5/BI OR 411241-20-8/BI OR 4701-17-1/BI OR  
51110-01-1/BI OR 51992-85-9/BI OR 59090-17-4/BI OR 6318-16-7/BI  
OR 64-17-5/BI OR 9011-97-6/BI)  
L13 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 AND L9  
L14 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 OR L9  
L15 24 SEA FILE=REGISTRY ABB=ON PLU=ON (AZIDE/CN OR "AZIDE (H(N3)21-  
)" /CN OR "AZIDE (H(N3)21-), TETRAPHENYLPHOSPHONIUM" /CN OR  
"AZIDE (N3-)" /CN OR "AZIDE DIBENZYL DIMETHYLAMMONIUM" /CN OR  
"AZIDE ION" /CN OR "AZIDE ION(1-)" /CN OR "AZIDE RADICAL" /CN OR  
"AZIDE(1-)" /CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3  
-OXOOCTADECAXOCTADECANADATE(10-) (1:1)" /CN OR "AZIDE,  
COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3-OXOOCTADECAXOCTADECANAD  
ADATE(13-) (1:1)" /CN OR "AZIDE, LABELED WITH NITROGEN-15" /CN  
OR "AZIDE, MONOHYDRATE" /CN OR AZIDE-1-15N /CN OR AZIDE-15N2 /CN  
OR AZIDE-15N3 /CN OR AZIDE-2-15N /CN OR AZIDIAMANTANE /CN OR  
"AZIDIC ACID" /CN OR AZIDIN /CN OR AZIDIN-NAGANIN /CN OR AZIDINE /C  
N OR "AZIDINE FAST SCARLET 4BS" /CN OR "AZIDINE FAST SCARLET  
7BS" /CN OR "AZIDINE FAST SCARLET GGS" /CN OR "AZIDINE YELLOW  
5G" /CN OR AZIDIOL /CN OR AZIDITHION /CN OR AZIDO /CN OR "AZIDO  
RADICAL" /CN)  
L16 16 SEA FILE=REGISTRY ABB=ON PLU=ON "AZIDE" AND L15  
L18 545 SEA FILE=REGISTRY ABB=ON PLU=ON "AZID"  
L19 3867 SEA FILE=HCAPLUS ABB=ON PLU=ON L16  
L20 36392 SEA FILE=HCAPLUS ABB=ON PLU=ON L18  
L21 141428 SEA FILE=HCAPLUS ABB=ON PLU=ON (N3 OR ?AZID? OR NITRENE OR  
SINGLET OXYGEN)  
L22 2611 SEA FILE=HCAPLUS ABB=ON PLU=ON DYE(L) (L19 OR L20 OR L21)  
L29 163257 SEA FILE=HCAPLUS ABB=ON PLU=ON (SOMATOSTATIN OR BACTERIOENDOT  
OXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)  
L44 318 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPOCRELLIN?  
L45 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L44  
L46 65735 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPOCRELLIN? OR AZO OR  
METHINE OR INDOLENIUM  
L47 429 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L46  
L48 429 SEA FILE=HCAPLUS ABB=ON PLU=ON L47 AND DYE

CEPERLEY 09/898,885

L50	1	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L48 AND L29
L51	345	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L22(L)L46
L52	1	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L51 AND L29
L53	5	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L51 AND CONJUGAT?
L55	11	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L50 OR L52 OR L45 OR L53
L56	11	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L55 NOT (L13 OR L14)



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L56 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:864441 HCAPLUS

DOCUMENT NUMBER: 136:196250

TITLE: Butylamino-demethoxy-**hypocrellins** and photodynamic therapy decreases human cancer in vitro and in vivo

AUTHOR(S): Xu, Shangjie; Chen, Shen; Zhang, Manhua; Shen, Tao; Zhao, Yupei; Liu, Ziwen; Wu, Yuande

CORPORATE SOURCE: Center for Molecular Sciences, Chinese Academy of Sciences, Institute of Chemistry, Beijing, 100080, Peop. Rep. China

SOURCE: Biochimica et Biophysica Acta (2001), 1537(3), 222-232

CODEN: BBACAQ; ISSN: 0006-3002

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 2-Butylamino-2-demethoxy-**hypocrellin** A (BAHA) and B (BAHB) are new photosensitizers synthesized by a mild reaction of **hypocrellins** and butylamine. In BAHA and BAHB, the peri-hydroxylated perylenequinone structure of the parent **hypocrellins** is preserved and the red absorption is enhanced distinctly. ESR spin trapping measurements and 9,10-diphenylanthracene bleaching studies were used to investigate the photodynamic action of BAHA and BAHB in the presence of oxygen. **Singlet oxygen** ( $^1O_2$ ) and superoxide anion radical ( $O_2^{\cdot-}$ ) produced by illuminating BAHA and BAHB in aerobic soln. have been obsd. Compared with **hypocrellin** A and B, BAHA and BAHB primarily remained able to generate  $^1O_2$  and enhanced distinctly the  $O_2^{\cdot-}$ -generating abilities. The photodynamic action of BAHA and BAHB in the therapy of cancer was investigated in vitro and in vivo. Both in vitro and in vivo results revealed a significant decrease in cancer cell growth. Laser or **dye** alone had no effect, indicating that intratumor BAHA and laser therapy may prove useful in unresectable cancer.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=&gt; d ibib abs 2

L56 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:255871 HCAPLUS  
 DOCUMENT NUMBER: 134:287949  
 TITLE: Optical recording medium comprising the  
 metal-containing azo dye  
 INVENTOR(S): Suzuki, Yuki; Horie, Michikazu; Maeda, Syuichi;  
 Kurose, Yutaka; Okamoto, Yuko  
 PATENT ASSIGNEE(S): Mitsubishi Chemical Corporation, Japan  
 SOURCE: U.S., 38 pp., Cont.-in-part of U.S. Ser. No. 892,338,  
 abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6214519	B1	20010410	US 1998-33654	19980303
JP 09058123	A2	19970304	JP 1995-213501	19950822
JP 09274732	A2	19971021	JP 1996-81398	19960403
JP 10006644	A2	19980113	JP 1996-159843	19960620
PRIORITY APPLN. INFO.:			JP 1995-213501	A 19950822
			JP 1995-235132	A 19950913
			JP 1996-4644	A 19960116
			JP 1996-81398	A 19960403
			JP 1996-159843	A 19960620
			US 1996-701741	B2 19960822
			US 1997-892338	B2 19970714
OTHER SOURCE(S):			MARPAT 134:287949	
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB An optical recording medium comprising a transparent substrate and at least a recording layer contg. an org. dye, a reflecting metal layer and a protective layer sequentially laminated on the substrate in this order, which has the following characteristics (a) to (c): (a) the substrate has a tracking groove with a track pitch of from 0.7 to 1.0  $\mu\text{m}$  and the recording layer shows a modulation amplitude of EFM signal of at least 50% when recording is carried out by a laser beam with a wavelength of from 600 to 700 nm, and has a reflectance of from 45 to 65%; (b) in a thermogravimetric anal. of the dye, the inclination of the wt. redn. to the temp. in the main wt. redn. process is at least 2%/C.degree.; and (c) in the thermogravimetric anal. of the dye, the total wt. redn. in the main wt. redn. process is at least 25%. The optical recording medium also comprising the azo chelate dye of formula I-VI (X1 = electron attractive group substituent which is **conjugative** with the diazo group of the formula I or II; Y1 = OH, COOH, SO<sub>3</sub>M (M = H, or an alk. metal); R1, R2, R3, R4 = Cl-6 alkyl; Z = H, halogen or Cl-3 alkyl; X2 = H, Cl-6 alkyl or C3-6 cycloalkyl; Y2 = alkyl).

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L56 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2002 ACS  
 IC ICM B41M005-26  
 NCL 430270160  
 CC 74-12 (Radiation Chemistry, Photochemistry, and Photographic and Other Reprographic Processes)  
 ST optical recording laser disk metal contg azo dye prepn  
 IT Azo dyes  
 Erasable optical disks  
 (optical recording medium comprising metal-contg. azo dye)  
 IT 28106-65-2, Tetrafluoropropanol 39660-55-4, Octafluoropentanol  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (metal-contg. azo dye dissolved in fluorinated alc. with b.p. from 110.degree. to 150.degree.C for prepn. of optical recording medium)  
 IT 186818-73-5 189028-01-1 198084-88-7 198084-92-3 198992-10-8  
 265093-56-9 333725-53-4 333725-62-5 333754-15-7 333754-16-8  
 RL: DEV (Device component use); PRP (Properties); USES (Uses)  
 (optical recording medium comprising metal-contg. azo dye)  
 IT 333725-54-5P 333725-55-6P 333725-56-7P 333725-57-8P 333725-58-9P  
 333725-59-0P 333725-60-3P 333725-61-4P  
 RL: DEV (Device component use); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)  
 (optical recording medium comprising metal-contg. azo dye)  
 IT 18007-64-2 25470-94-4 202604-90-8 330680-81-4  
 RL: DEV (Device component use); PRP (Properties); USES (Uses)  
 (optical recording medium comprising metal-contg. azo dye and mixt. of dyes)  
 IT 199128-40-0, EX 318 218949-24-7, SD 318  
 RL: DEV (Device component use); USES (Uses)  
 (optical recording medium comprising metal-contg. azo dye and protecting layer made of)  
 IT 7440-22-4, Silver, uses  
 RL: DEV (Device component use); USES (Uses)  
 (optical recording medium comprising metal-contg. azo dye and reflecting layer consisted of)  
 IT 27115-74-8P, 2-Amino-5-isopropyl-1,3,4-thiadiazole 204056-75-7P  
 204056-77-9P 204056-79-1P 333723-84-5P  
 RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. of metal-contg. azo dyes for optical recording medium)  
 IT 79-19-6, **Thiosemicarbazide** 79-31-2, Isobutyric acid 91-68-9,  
 N,N-Diethyl-3-aminophenol 14068-53-2, 2-Amino-5-ethyl-1,3,4-thiadiazole  
 17467-35-5, 5-Amino-3-methyl-1,2,4-thiadiazole 39222-73-6,  
 2-Amino-5-tert-butyl-1,3,4-thiadiazole 43141-69-1, N,N-Dibutyl-3-aminophenol  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prepn. of metal-contg. azo dyes for optical recording medium)  
 IT 6018-89-9, Nickel acetate tetrahydrate  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prepn. of nickel-contg. azo dyes for optical recording medium)

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L56 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:554335 HCAPLUS  
 DOCUMENT NUMBER: 133:263274  
 TITLE: Synthesis and EPR investigations of new aminated  
**hypocrellin** derivatives  
 AUTHOR(S): He, Y.-Y.; Jiang, L.-J.  
 CORPORATE SOURCE: Institute of Chemistry, Center for Molecular Sciences,  
 Academia Sinica, Beijing, Peop. Rep. China  
 SOURCE: Free Radical Biology & Medicine (2000), 28(11),  
 1642-1651  
 CODEN: FRBMEH; ISSN: 0891-5849  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB **Hypocrellins** are novel photodynamic agents. A recent advance in the synthesis of **hypocrellin** congeners results in the prodn. of two amino-substituted **hypocrellin** B derivs. in high yield via photochem. reaction. Both compds. exhibit similar photodynamic activity as **hypocrellin** B in terms of type I and type II mechanisms. In anaerobic media, semiquinone anion radicals can be detected by ESR (EPR) under irradiation; while superoxide anion radical, hydroxyl radical and **singlet oxygen** are photoproduced when oxygen was present. The quantum yields of **singlet oxygen** by these two new compds. are detd. to be 0.72 and 0.64, resp., similar to that of **hypocrellin** B. The comparison of the photosensitization chem. of compds. 1 and 2 in liposomes with that in homogeneous soln. has also been made. In liposomes, the type II photoprocess was favored and predominant over the type I photoprocess due to the decreased interactions between **dye** mols. Both compds. exhibit much stronger red light absorption than the parent **hypocrellin** and therefore, merit investigation as photosensitizers.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L56 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2002 ACS  
 CC 8-9 (Radiation Biochemistry)  
 ST **hypocrellin** deriv synthesis photosensitizer photodynamic therapy liposome  
 IT Drug delivery systems  
 (liposomes; synthesis and EPR investigations of new aminated **hypocrellin** derivs.)  
 IT Photodynamic action  
 Photodynamic therapy  
 Photosensitizers (pharmaceutical)  
 (synthesis and EPR investigations of new aminated **hypocrellin** derivs.)  
 IT 7782-44-7, Oxygen, formation (nonpreparative)  
 RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)  
 (singlet; synthesis and EPR investigations of new aminated **hypocrellin** derivs.)  
 IT 123940-54-5DP, **Hypocrellin** B, derivs. 200722-94-7P  
 200723-03-1P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)  
(synthesis and EPR investigations of new aminated **hypocrellin**  
derivs.)

IT 3225-30-7, Semiquinone radical 3352-57-6, Hydroxyl radical, formation  
(nonpreparative) 11062-77-4, Superoxide anion  
RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)  
(synthesis and EPR investigations of new aminated **hypocrellin**  
derivs.)

IT 60-23-1, Cysteamine 77029-83-5, **Hypocrellin a**  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(synthesis and EPR investigations of new aminated **hypocrellin**  
derivs.)

=&gt; d ibib abs 4

L56 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:729270 HCAPLUS

DOCUMENT NUMBER: 132:32708

TITLE: Pharmacokinetics, tissue distribution and photodynamic therapy efficacy of liposomal-delivered **hypocrellin A**, a potential photosensitizer for tumor therapy

AUTHOR(S): Wang, Zhi-Jin; He, Yu-Ying; Huang, Chao-Guo; Huang, Jin-Sheng; Huang, Ying-Cai; An, Jing-Yi; Gu, Ying; Jiang, Li-Jin

CORPORATE SOURCE: Laser Center, Department of Gastrointestintology, PLA 305 Hospital, Beijing, Peop. Rep. China

SOURCE: Photochemistry and Photobiology (1999), 70(5), 773-780  
CODEN: PHCBAP; ISSN: 0031-8655

PUBLISHER: American Society for Photobiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Hypocrellin A**, from *Hypocrella bambusae*, is a novel photosensitizer of high **singlet oxygen** quantum yield for photodynamic therapy (PDT). Tissue distributions were studied in tumor-bearing mice as a function of time following administration. The tumor model was S-180 sarcoma transplanted into one hind leg of male Kunming mice; **hypocrellin A** (HA) was delivered to the mice by i.v. injection of 5 mg/kg of body wt. as a suspension either as a unilamellar liposome or in DMSO (DMSO)-solubilized saline. The HA was isolated from several tissues and organs, as well as tumors and peritumoral muscles and skin. Quantitation was performed by a high-performance liq. chromatog. technique with detection that utilizes the native fluorescence of HA. Independent of the delivery system, the **dye** was retained in tumors at higher concns. than in normal tissues, except for kidney, liver, lung and spleen. The **dye** retention in tumors was high and was vehicle dependent. For the liposomal system, the maximal accumulation in tumor and maximal ratios of **dye** in tumor vs. peritumoral muscle and skin occurred 12 h post-injection; for the DMSO saline system, the maximal ratio occurred earlier, 6 h postadministration. Liposomal delivery improved the selective accumulation of the **dye** in tumor with higher maximal levels in tumor and higher ratios of tumor-to-muscle and tumor-to-skin. Levels of **dye** were very low or not detectable in the brain. The PDT efficacy of HA in the liposome and DMSO saline systems was detd. by evaluating the tumor vol. regression percent. The PDT efficacy of HA in liposomes was highest when light treatment was performed at 12 h postinjection, consistent with the highest retention of HA in tumors. Similarly, the maximal PDT efficacy in DMSO saline was attained at 6 h postinjection, the highest HA retention point in tumor. Moreover, the peak PDT efficacy of HA in liposomes was much higher than that of HA in DMSO saline and even hematoporphyrin monomethylether.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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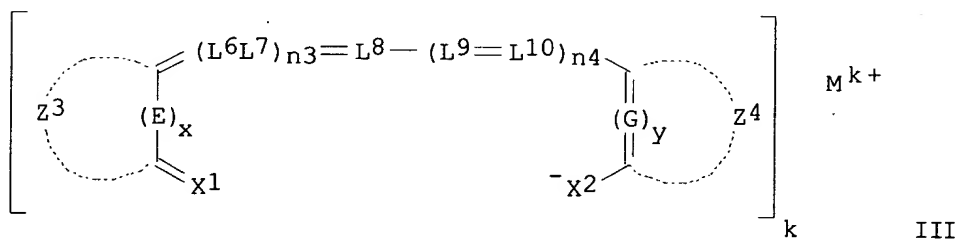
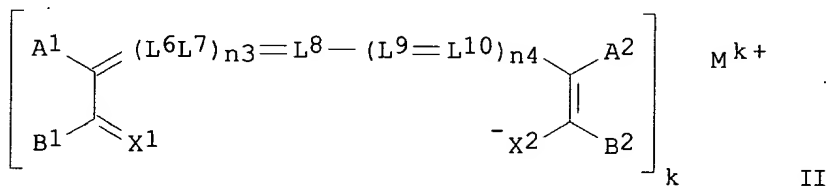
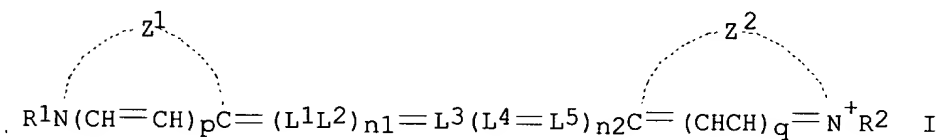
L56 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1999:716768 HCAPLUS  
DOCUMENT NUMBER: 132:46999  
TITLE: Photodynamic action of **hypocrellin** dyes:  
structure-activity relationships  
AUTHOR(S): He, Yu-Ying; Liu, Hong-Yan; An, Jing-Yi; Han, Rei;  
Jiang, Li-Jin  
CORPORATE SOURCE: Institute of Photographic Chemistry, Academia Sinica,  
Beijing, 100101, Peop. Rep. China  
SOURCE: Dyes and Pigments (1999), 44(1), 63-67  
CODEN: DYPIDX; ISSN: 0143-7208  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB **Hypocrellin** and its derivs. were compared for their photodynamic  
effects on human oral cavity epithelial carcinoma KB cell line. The  
amphiphilicity as well as the **singlet oxygen**  
generating quantum yield of the **hypocrellin dyes**  
affected their photodynamic activity. The most hydrophilic **dyes**  
exhibited the lowest phototoxic activity, whereas the hydrophobic and  
amphiphilic **dyes** with higher **singlet oxygen**  
-generating quantum yield, exhibited high photodynamic activity.  
Cysteamine mono- and di-substituted **hypocrellin B** and cysteine  
mono-substituted **hypocrellin B**, demonstrating strong red  
absorption in the domain of phototherapeutic window (600-900 nm), proper  
hydrophobic and amphiphilic properties and high photocytotoxicity to KB  
cells, might prove to be potential phototherapeutic agents.  
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L56 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1999:147611 HCAPLUS  
 DOCUMENT NUMBER: 130:202986  
 TITLE: Optical information recording material and recording method  
 INVENTOR(S): Wariishi, Koji  
 PATENT ASSIGNEE(S): Fuji Photo Film Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 51 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11058973	A2	19990302	JP 1997-238962	19970820

GI



AB The title recording material has a recording layer contg. a cyanine **dye** I (Z1, Z2 = atoms required to form 5-6-membered N-contg. ring; R1, R2 = alkyl; L1-5 **methine**; n1, n2, p, q = 0, 1; M1 = counter ion, m1 = integer for neutralizing the charge) and a oxonol **dye** with proton or an onium ion II and/or III (A1, A2, B1, B2 = substituent; Z3, Z4 = atoms required to form hydrocarbon or heterocyclyl ring; E, C = atoms required to form **conjugated** double bond chain; X1 = :O, :NR, :C(CN)2; X2 = O, NR, C(CN)2; L6-10 = **methine**; Mk+ = proton, onium ion; n3, n4 = 0-2; x, y = 0, 1; k = 1-10). The invention recording material is suitable for the high-speed reading.



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L56 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2002 ACS  
 IC ICM B41M005-26  
 ICS G11B007-00; G11B007-24  
 CC 74-12 (Radiation Chemistry, Photochemistry, and Photographic and Other  
 Reprographic Processes)  
 ST optical recording material cyanine oxonol dye  
 IT Cyanine dyes  
 (contained in recording layer for optical recording material and  
 method)  
 IT Optical recording materials  
 (laser; having recording layer contg. specified cyanine and oxonol dye)  
 IT Dyes  
 (oxonol; contained in recording layer for optical recording material  
 and method)  
 IT 54389-98-9 121482-73-3 142315-00-2 189189-12-6 192587-99-8  
 194938-05-1 220672-28-6  
 RL: TEM (Technical or engineered material use); USES (Uses)  
 (cyanine dye contained in recording layer for optical recording  
 material and method)  
 IT 205817-34-1 205817-36-3 205817-39-6 217963-64-9 220672-30-0  
 220672-31-1 220672-33-3 220672-37-7 220672-38-8 220672-39-9  
 RL: TEM (Technical or engineered material use); USES (Uses)  
 (oxonol dye contained in recording layer for optical recording material  
 and method)

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L56 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1993:665415 HCAPLUS  
 DOCUMENT NUMBER: 119:265415  
 TITLE: Photosensitized oxidation of bilirubin in serum  
 AUTHOR(S): Cao, Enhua; Li, Yuke; Wang, Jujun  
 CORPORATE SOURCE: Inst. Biophys., Acad. Sin., Beijing, 100101, Peop.  
 Rep. China  
 SOURCE: Shengwu Wuli Xuebao (1993), 9(1), 158-62  
 CODEN: SWXUEN; ISSN: 1000-6737  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Chinese  
 AB A deriv. of perylenequinone, **hypocrellin B** (HC-B), was shown as  
 a photodynamic **dye**, to accelerate the photooxidn. of bilirubin  
 in serum with an increase in the oxidative rate of >5-fold. Studies of  
 the effect of various active oxygen quenchers on HC-B photosensitized  
 oxidn. of bilirubin indicated that in serum, both free radical reactions  
 (Type I) and **singlet oxygen** reaction (Type II) seem to  
 occur simultaneously.

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L56 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:577151 HCAPLUS  
 DOCUMENT NUMBER: 115:177151  
 TITLE: Evaluation of the newborn mouse model for chemical  
 tumorigenesis  
 AUTHOR(S): Fujii, Keiji  
 CORPORATE SOURCE: Inst. Basic Med. Sci., Univ. Tsukuba, Tsukuba, 305,  
 Japan  
 SOURCE: Carcinogenesis (London) (1991), 12(8), 1409-15  
 CODEN: CRNGDP; ISSN: 0143-3334  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB A total of 45 chems., including 2 arom. hydrocarbons, 5 arom. amines, 3 **azo dyes**, 10 nitroso compds., 3 **steroids**, 4 tryptophan metabolites and their related compds., 4 naturally occurring substances, 4 pyrolyzates of amino acids, and 10 misc. compds., were tested for newborn mouse tumorigenesis assay (NMTA). The results of the NMTA were compared with data from Survey of Compds. Which Have Been Tested for Carcinogenic Activity, NIH, NCI, USA (SCWHBTCA), and also with data from the IARC Monographs (Vols 1-41), Lyon, France (IARC). Of the 45 chems. tested by the NMTA, 28 chems. showed pos. results in the NMTA, and the remaining 17 chems. were neg. for tumor development. The correlation of the results between the NMTA and the mouse and/or rat carcinogenesis test starting at young adult age reported in the SCWHBTCA and in the IARC were compared with 37 chems. tested; the remaining 8 chems. were found only in NMTA results. Therefore, 31 of 37 chems. (83.8%) tested by the NMTA showed similar carcinogenic or non-carcinogenic results obtained in adult mouse and/or rat carcinogenesis tests. The remaining 6 chems. showed contradictory results between the NMTA and adult mouse and/or rat carcinogenesis tests. Those 6 chems. were N-hydroxy-4-acetylamino-biphenyl, estradiol, 3-hydroxyanthranilic acid, 3-hydroxy-L-kynurenine, isonicotinic acid **hydrazide**, and phenobarbital. Among the 37 chems., 34 were comparable with the results of the adult mouse carcinogenesis test and those of the NMTA. Twenty-nine of 34 chems. (85.3%) showed similar results to the adult mouse carcinogenesis test. Contradictory results were obtained with the following 5 chems.: N-hydroxyacetylamino-biphenyl, 3-hydroxyanthranilic acid, 3-hydroxy-L-kynurenine, isonicotinic acid **hydrazide** and phenobarbital. There were 35 chems. which were comparable with the results of the adult rat carcinogenesis test, and 32 chems. showed the same results as the NMTA (91.4%). Dissimilar results were obtained with the following 3 chems.: estradiol, 3-hydroxyanthranilic acid and phenobarbital. Thus, the NMTA is one of the most useful and reliable methods for detecting tumorigenic or non-tumorigenic chems., when a small amt. of chem. is available for rodent carcinogenesis test and the duration of the study is limited to 1 yr.

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L56 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1978:542885 HCAPLUS

DOCUMENT NUMBER: 89:142885

TITLE: Selective removal of albumin from blood fluids

INVENTOR(S): Travis, James; Pannell, Ralph

PATENT ASSIGNEE(S): Research Corp., USA

SOURCE: U.S., 8 pp. Cont.-in-part of U.S. 4,016,149.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4093612	A	19780606	US 1976-661890	19760227
US 4016149	A	19770405	US 1975-601676	19750804
PRIORITY APPLN. INFO.:			US 1973-396036	19730910
			US 1975-601676	19750804
			FR 1974-30595	19740910
			IT 1974-27141	19740910

AB Albumins are selectively removed from aq. fluids (blood plasma or serum) by use of adsorbents prepd. by coupling reactive **dyes** to solid supports. All **dyes** have the general sulfanilido-**triazidinyl**-sulfoaryl group, wherein the aryl groups are Ph or naphthyl, and the general group is bonded further to aryl groups via an amino or **azo** linkage. The support phases include agarose (Sephacrose), polyacrylamides, and acrylic resins. By use of such **conjugates**, albumins may be sepd. without denaturation, and the **conjugates** may be regenerated and used without loss of activity. Thus, 100-mL Sepharose 4B was treated with aq. CNBr (16 g) at pH 11 and 10.degree. for 5 h. The supernatant was decanted, and the Sepharose was mixed with 0.1M NaHCO<sub>3</sub> (pH 9.5), which then was decanted. Blue Dextran (1g) in 100 mL of the NaHCO<sub>3</sub> buffer was added to the Sepharose for 24 h at 4.degree.. After decantation of the supernatant, the Sepharose-Blue Dextran **conjugate** was washed, suspended in buffer contg. 0.05M Tris-HCl (pH 8) and 0.5M NaCl, and packed into a 1 .times. 20 cm chromatog. column. When 2 mL plasma was applied to this column, 96% of the albumin was adsorbed, whereas .gtoreq.84% of each of all the other proteins studied was eluted in buffer. Albumin was desorbed by washing the column with 0.05M Tris-HCl (pH 8) contg. 0.3M NaSCN, and the column was regenerated by washing with 0.05M Tris-HCl (pH 8) contg. 0.05M NaCl. Albumin of >98% purity was obtained.

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L56 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1963:436049 HCAPLUS

DOCUMENT NUMBER: 59:36049

ORIGINAL REFERENCE NO.: 59:6542e-h, 6543a-d

TITLE: Aromatic azo and disazo compounds. LII. Increasing the yields of the coupling reaction by the addition of thiosulfate. Chain mechanism of arylation

AUTHOR(S): Allan, Z. J.; Podstata, J.

CORPORATE SOURCE: Vyzkumny Ustav Org. Synthes, Pardubice-Rybitvi

SOURCE: Collection Czech. Chem. Commun. (1963), 28, 349-65

DOCUMENT TYPE: Journal

LANGUAGE: German

GI For diagram(s), see printed CA Issue.

AB cf. CA 59, 6410h. Side reactions, including arylation and elimination of N<sub>2</sub>, occurring in the coupling of diazotized o-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>H (I), 3,4-H<sub>2</sub>N(HO)C<sub>6</sub>H<sub>3</sub>SO<sub>3</sub>H, and p-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H with o-C<sub>6</sub>H<sub>4</sub>(OH)<sub>2</sub>, o-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>OH, 1,5-C<sub>10</sub>H<sub>6</sub>(OH)<sub>2</sub>, and 1,7,3-(HO)<sub>2</sub>C<sub>10</sub>H<sub>5</sub>SO<sub>5</sub>H (II), were suppressed by the addn. of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and this resulted in an increased stability of the diazo compd. in the reaction mixt. and raised the yields to 60-97%. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> interrupts the chain arylation reaction at an early stage. All coupling components affected by the action of Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> possess two OH or NH<sub>2</sub> groups in **conjugation** and are thus able to form corresponding quinones and semiquinones. Small amts. of semiquinone in the mixt. react with the diazo compd. to yield arylsemiquinones that convert another hydroquinone into semiquinone and this starts a chain reaction. Expts. with 11 diazotized amines revealed that II couples preferentially in the 2-position, owing to the higher pK of the 1-OH group influenced by the SO<sub>3</sub>H group. Preferential **azo** coupling in the 2-position increases with the electrophilicity of the diazo compd., so that coupling of o- and p-NH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>NO<sub>2</sub> forms practically no 8-arylazo isomer. Prepn. of 2 **azo dyes** is described. Thus, 13.7 g. I diazotized, neutralized to Congo red (final vol. 500 ml.), added in 5 min. at 0.degree. to a soln. of 4.3 g. II, 150 g. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>.5H<sub>2</sub>O, and 28.5 ml. 26.5% NH<sub>4</sub>OH in H<sub>2</sub>O made up to 500 ml., the brown ppt. of the **dye** treated at 10.degree. with 35.5 g. NaCl, stirred 2 hrs., the ppt. filtered, washed at 10.degree. with 250 ml. 9% NaCl soln. and dried at 90.degree. gave 34.5 g. chromatographically homogenous 3-(2-carboxyphenylazo)-4,6-dihydroxy-2-naphthalenesulfonic acid (III), while the filtrate boiled 15 min. with 9 g. CaCl<sub>2</sub> yielded 14 g. red ppt. contg. 30 millimoles 5-(2-carboxyphenylazo) isomer of III. Coupling of III with a 2nd mol. of the diazo compd. requires addn. of pyridine and Cu<sup>2+</sup>, since pyridine facilitates the proton cleavage at the site of coupling in case of a steric hindrance by a SO<sub>3</sub>H group in the 3-position. The binding of O on bivalent Cu in the complex of III is strongly polarized which strengthens the neg. charge of O and also at the coupling sites. Thus, 0.1 mole tetrazotized benzidine coupled with 0.108 mole o-HOC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>H in NaHCO<sub>3</sub> soln. at 0-3.degree., the suspension poured with ice-cooling into a soln. of 50.8 g. III in 38 ml. 1.25M Na<sub>2</sub>CO<sub>3</sub>, 25 g. CuSO<sub>4</sub>.5H<sub>2</sub>O and 209 ml. pyridine in 190 ml. 1.25M Na<sub>2</sub>CO<sub>3</sub> soln. added, the mixt. made up to 1.5 l. with water, cooled with 1 kg. ice, stirred overnight with a gradual rise of temp. to 20.degree., the suspension heated to 70.degree., 800 g. NaCl added and the ppt. filtered gave IV, which **dyes** cotton olive-yellow and is fast to light, washing, perspiration, and alkali. LIIII. Mutual conversion of cis and trans diazotates; the catalytic effect of cellulose and the photochemical effect of light. V. Chmatal and Z. J. Allan. Ibid. 366-76. Cis diazotates of PhNH<sub>2</sub>, p-ClC<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, m- and p-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CO<sub>2</sub>H, m- and p-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H, m- and

p-H<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>NO<sub>2</sub> are instantaneously isomerized to trans diazotates on contact with cellulose, silica gel, Al silicates, and, to a lesser extent, with glass fibers, with triazene derivs. as side-products. The ratio of trans diazotate to triazenes increases with increasing electron-withdrawing activity of the substituent. Trans diazotates in 0.1N NaOH, triazenes in alk. and neutral medium, diazonium salts in acid medium, and **quinonediazides** in dil. NaOH are stable towards cellulose and can be chromatographed on paper. Photochem. isomerization of cis diazotates to the transform is reversible and results in an equil. The effect of the substituents on the reaction rate is opposite to that in thermal isomerization. The reaction mechanisms are discussed.

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L56 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1962:436204 HCAPLUS

DOCUMENT NUMBER: 57:36204

ORIGINAL REFERENCE NO.: 57:7198a-i,7199a-b

TITLE: o-Quinones. XX. The effect of substituents on the polarity of the carbonyl groups in o-benzoquinones

AUTHOR(S): Horner, Leopold; Duerckheimer, Walter

CORPORATE SOURCE: Univ. Mainz, Germany

SOURCE: Ber. (1962), 95, 1206-18

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

GI For diagram(s), see printed CA Issue.

AB cf. CA 56, 8560g. A series of mono- and disubstituted o-benzoquinones with p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>NHNH<sub>2</sub> (I) was converted to the corresponding o-quinone **diazides**. The participation of the CO groups in the o-quinone in the reaction was detd. from the ratio of the isomeric phenols obtained by reductive exchange of the diazo group, o-Quinones with Me, Me<sub>3</sub>C, Cl, MeO, and PhCH<sub>2</sub>O in the 4- or 5-position react preferentially on the CO group which is not in **conjugation** with the substituent. In 3- and 6-substituted o-benzoquinones steric interactions are more predominant than the mesomeric and inductive substituent effects; the CO group in the m-position to the 3- or 6-substituent reacts preferentially or exclusively. The appropriate benzoquinone in CH<sub>2</sub>Cl<sub>2</sub> cooled to -15.degree., treated at 0.degree. with I in CH<sub>2</sub>Cl<sub>2</sub>, refrigerated 1 hr., concd. to 1/4 vol., and chromatographed on Al<sub>2</sub>O<sub>3</sub> gave the corresponding o-benzoquinone **diazide** in mixt. with an isomeric product which couples in alk. soln. with m-C<sub>6</sub>H<sub>4</sub>(OH)<sub>2</sub>, 1,3,5-C<sub>6</sub>H<sub>3</sub>(OH)<sub>3</sub>, and 2-C<sub>10</sub>H<sub>7</sub>OH to red **azo dyes** and gives with HClMeOH the HCl salt. In this manner were prepd. the following compds. (m.p., g.-yield, g.-amts. appropriate quinone and I and cc. vols. used for quinone and I given): o-benzoquinone **diazide** (II), 63-4.degree., 0.85, 2.16, 3.72, 80, 80; 4-Me deriv. (III) of II, 70-1.degree., 2.0-2.25, 4.9, 5.5, 130, 100; 4-Me<sub>3</sub>C deriv. (IV) of II, 60-1.degree., 1.4-1.5, 3.28, 3.72, 70, 70; 4-MeO deriv. (V) of II, 103-4.degree., 1.4-1.9, 2.76, 3.72, 70, 70; 4-PhCH<sub>2</sub>O deriv. (VI), 119-20.degree., 1.50, 2.14, 1.86, 40, 40; 4-Cl deriv. (VII) of II, about 112.degree., 1.2-1.45, 2.85, 3.72, 100, 70; 3-MeO deriv. (VIII) of II, 107-8.degree., 0.6-0.7, 2.76, 100, 3.72, 70; VIII, 107-8.degree., 0.42, 2.76, 1.7, -, - (50 cc. dioxane); 3-Cl deriv. (IX) of II, 99-100.degree., 0.82, 1.43, 1.86, 40, 40; 4,5-di-Me deriv. (X) of II, 62-3.degree., 1.1, 2.72, 3.72, 50, 80; 3,5-di-Me deriv. (XI), 83-4.degree., 1.2-1.4, 2.72, 3.72, 60, 80; 3,5-di-Me<sub>3</sub>C deriv. (XII) of II, 75-6.degree., 3.9, 4.4, 3.8, -(50 cc. MeOH), -; 4,5-di-Cl deriv. (XIII) of II, -, 0.91, 1.77, 1.86, 50, 40. In the prepn. of VIII, dihydroxymethoxydiphenyl sulfone, m. 204.degree. (aq. MeOH), was also obtained. Tetrachloro-o-quinone (XIV) (2.45 g.) in 30 cc. CH<sub>2</sub>Cl<sub>2</sub> treated slowly with shaking with 1.86 g. II in 50 cc. CH<sub>2</sub>Cl<sub>2</sub> yielded 1.70 g. o-(p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>)C<sub>6</sub>Cl<sub>4</sub>OH, m. 164-5.degree. (aq. MeOH). XIV (2.5 g.) in 20 cc. AcOH treated with shaking with 1 g. BzNHNH<sub>2</sub> and filtered after 1 hr. yielded 0.70 g. XV; it sublimes from 240.degree. on without decompn.; it gives a red-violet soln. in aq. Na<sub>2</sub>CO<sub>3</sub> and 2N NaOH. I (1.0 g.) in 20 cc. MeOH treated slowly with shaking with 1.2 g. 4-methyl-o-quinone, refrigerated 1 hr., and dild. with 2 vols. H<sub>2</sub>O gave p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub> deriv., m. 164.degree. (aq. MeOH); it gives a green enol reaction with FeCl<sub>3</sub>. The appropriate unsym. o-quinone **diazide** (contg. an isomeric by-product) in EtOH treated with concd. HCl and 50% aq. H<sub>3</sub>PO<sub>2</sub>, kept 2 days at room temp., and evapd. in vacuo in the dark, the residue dild. with 30-50 cc. H<sub>2</sub>O and extd. 6 hrs. with Et<sub>2</sub>O, and the ext. distd. yielded a

mixt. of 2 isomeric phenols. The following compds. were reduced in this manner (g.-amt. quinone ~~diazide~~ mixt. and cc. vols. EtOH, concd. HCl, and 50% aq. H<sub>3</sub>PO<sub>2</sub> used, b.p. range/ mm. of the resulting phenol mixt., g.-amt. of product obtained, and constituents and their % content of the resulting isomeric phenol mixt. given): III, 2.68, 20, 5, 16, 110-15.degree./12, 1.31, m-MeC<sub>6</sub>H<sub>4</sub>OH, 88, p-MeC<sub>6</sub>H<sub>4</sub>OH, 12; IV, 1.76, 30, 3, 15, about 120.degree./12, 0.72, m-Me<sub>3</sub>CC<sub>6</sub>H<sub>4</sub>OH, 80-5, pMe<sub>3</sub>CC<sub>6</sub>H<sub>4</sub>OH, 10-15; IV, 1.5, 25, 3, 12, 125.degree./20, 0.63, m-MeOC<sub>6</sub>H<sub>4</sub>OH, 98.8, p-MeOC<sub>6</sub>H<sub>4</sub>OH, 1.2; VII, 1.55, 30, 4, 15, 95-105.degree./20, 0.72, m-ClC<sub>8</sub>H<sub>4</sub>OH, 91.2, p-ClC<sub>6</sub>H<sub>4</sub>OH, 8.8; VIII, 1.5, 40, 2, 15, 120-5.degree./10, 1.05, guaiacol, 89.2, m-MeOC<sub>6</sub>H<sub>4</sub>OH, 32.4; VIII, 1.5, 40, 2, 15, 120-5.degree./10, 0.96, guaiacol, 67.6, m-MeOC<sub>6</sub>H<sub>4</sub>OH, 32.4; IX 1.54, 30, 4, 15, 100-20.degree./20, 0.23; o-ClC<sub>6</sub>H<sub>4</sub>OH, 89.3 (94.4), m-ClC<sub>6</sub>H<sub>4</sub>OH 10.7 (5.6); XI 1.48, 35, 4, 15, 105-15.degree./12, 0.65, 1,3,4-xyleneol, 93.3, 1,3,5-xyleneol, 6.7; XII, 2.32, 50, 2, 10, 150-5.degree./15, 1.63, 2,4-(Me<sub>3</sub>C)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>OH (XVI), 100 (m. 556.degree.), -, -. PhOH (9.6 g.) in 50 cc. Me<sub>3</sub>COH treated slowly with shaking with 30 cc. concd. H<sub>2</sub>SO<sub>4</sub> below 50.degree., kept overnight, and worked up yielded 10-11 g. XVI, b15 130-40.degree., m. 56-7.degree.. VIII (0.34 g.) and 0.56 g. V in 25 cc. EtOH treated with 2 cc. concd. HCl and 15 cc. 50% aq. H<sub>3</sub>PO<sub>2</sub> and worked up after 3 days yielded 0.42 g. mixt., b20 110-25.degree., of 43.4% guaiacol and 56.6% m-MeOC<sub>6</sub>H<sub>4</sub>OH.



=&gt; d que 165

L15 24 SEA FILE=REGISTRY ABB=ON PLU=ON (AZIDE/CN OR "AZIDE (H(N3)21- )"/CN OR "AZIDE (H(N3)21-), TETRAPHENYLPHOSPHONIUM"/CN OR "AZIDE (N3- )"/CN OR "AZIDE DIBENZYLDMETHYLAMMONIUM"/CN OR "AZIDE ION"/CN OR "AZIDE ION(1- )"/CN OR "AZIDE RADICAL"/CN OR "AZIDE(1- )"/CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3 -OXOOCTADECAXOOCTADECANADATE(10-) (1:1)"/CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3-OXOOCTADECAXOOCTADECANADATE(13-) (1:1)"/CN OR "AZIDE, LABELED WITH NITROGEN-15"/CN OR "AZIDE, MONOHYDRATE"/CN OR AZIDE-1-15N/CN OR AZIDE-15N2/CN OR AZIDE-15N3/CN OR AZIDE-2-15N/CN OR AZIDIAMANTANE/CN OR "AZIDIC ACID"/CN OR AZIDIN/CN OR AZIDIN-NAGANIN/CN OR AZIDINE/CN OR "AZIDINE FAST SCARLET 4BS"/CN OR "AZIDINE FAST SCARLET 7BS"/CN OR "AZIDINE FAST SCARLET GGS"/CN OR "AZIDINE YELLOW 5G"/CN OR AZIDIOL/CN OR AZIDITHION/CN OR AZIDO/CN OR "AZIDO RADICAL"/CN)

L16 16 SEA FILE=REGISTRY ABB=ON PLU=ON "AZIDE" AND L15

L18 545 SEA FILE=REGISTRY ABB=ON PLU=ON "AZID"

L19 3867 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

L20 36392 SEA FILE=HCAPLUS ABB=ON PLU=ON L18

L21 141428 SEA FILE=HCAPLUS ABB=ON PLU=ON (N3 OR ?AZID? OR NITRENE OR SINGLET OXYGEN)

L27 13956 SEA FILE=HCAPLUS ABB=ON PLU=ON RECEPTOR(5A) (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)

L40 55 SEA FILE=HCAPLUS ABB=ON PLU=ON (L19 OR L20 OR L21) (L) L27

L62 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L40 (L) CONJUGAT?

L63 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L40 AND CONJUGAT?

L64 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L40 AND (COVALENT? OR BOND? OR LINK?)

L65 27 SEA FILE=HCAPLUS ABB=ON PLU=ON (L62 OR L63 OR L64)

*L65 consists of azides conjugated  
to receptors of claim 2*

=&gt; d ibib abs 1-27

L65 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:677720 HCAPLUS

TITLE: Targeted Type 1 phototherapeutic agents using azido-peptide bioconjugates

AUTHOR(S): Rajagopalan, Raghavan; Achilefu, Samuel I.; Jimenez, Hermo N.; Webb, Elizabeth G.; Schmidt, Michelle A.; Bugaj, Joseph E.; Dorshow, Richard B.

CORPORATE SOURCE: Mallinckrodt, Inc., Saint Louis, MO, USA

SOURCE: Proc. SPIE-Int. Soc. Opt. Eng. (2001), 4259(Biomarkers and Biological Spectra Imaging), 129-132

CODEN: PSISDG; ISSN: 0277-786X

PUBLISHER: SPIE-The International Society for Optical Engineering

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Five peptides binding to **somatostatin** and **bombesin** **receptors** were **conjugated** to 4-azido -2,3,4,6-tetrafluorophenylbenzoic acid, a Type 1 photosensitizer, at the N-terminal position. The receptor affinities were detd. by competition binding assay using two different pancreatic tumor cell lines, CA20948 and AR42-J, that expresses **somatostatin-2** (SST-2) and **bombesin receptors** receptively. All compds. exhibited high receptor specificity, i.e., the IC50 values ranged between 1.0 to 64.0 nM. These **conjugates** may be useful for targeted Type 1 phototherapy via the generation of **nitrenes** at the cell surfaces expressing these receptors.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:659806 HCAPLUS

DOCUMENT NUMBER: 135:339429

TITLE: Nonradioactive photoaffinity labeling of steroid receptors using Western blot detection system

AUTHOR(S): Evans, Simon J.; Moore, Frank L.

CORPORATE SOURCE: Mental Health Research Institute, University of Michigan, Ann Arbor, MI, USA

SOURCE: Methods in Molecular Biology (Totowa, NJ, United States) (2001), 176(Steroid Receptor Methods), 261-272

CODEN: MMBIED; ISSN: 1064-3745

PUBLISHER: Humana Press Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors describes a novel strategy using a nonradioactive photoactive **steroid** ligand for labeling **steroid receptors**. Photoactive steroids can be synthesized by condensation reaction between the carboxyl group of a CMO-derivatized steroid and the amine group of an **azido-amine** catalyzed by a carbodiimide. A good **azido-amine** mol. for use with CMO-steroids is N-(2-aminoethyl)-4-**azido**-2-nitroaniline. The photolabel should be incubated with the receptor at sufficient concn. to achieve occupation of >90% of the receptor binding sites. A Western blot technique using a primary antibody directed against the steroid being studied is used for detection. A BSA-CMO-steroid **conjugate** can be used to optimize the system.

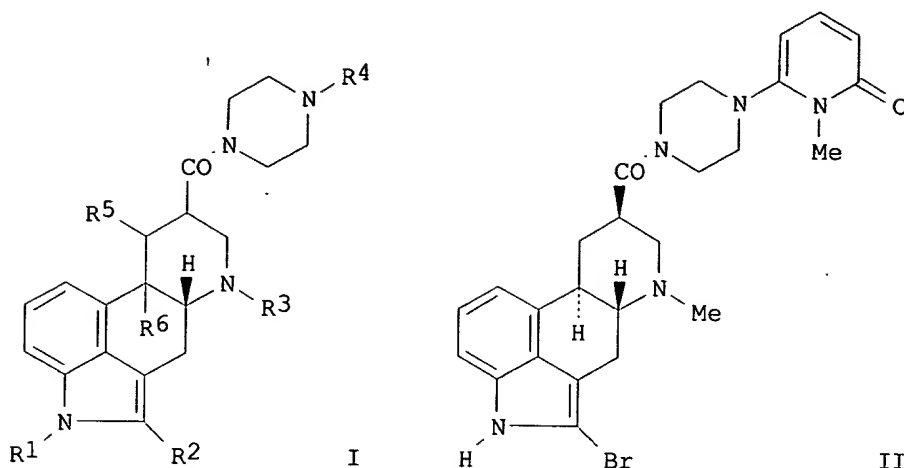
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:795015 HCAPLUS

DOCUMENT NUMBER: 130:25220  
 TITLE: Preparation of ergoline derivatives for pharmaceutical use  
 INVENTOR(S): Pfaeffli, Paul; Neumann, Peter; Swoboda, Robert; Stutz, Peter  
 PATENT ASSIGNEE(S): Novartis Ag, Switz.; Norvartis-Erfindungen Verwaltungsgesellschaft m.b.H.  
 SOURCE: PCT Int. Appl., 16 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854183	A2	19981203	WO 1998-EP3125	19980527
WO 9854183	A3	19990304		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9882108	A1	19981230	AU 1998-82108	19980527
AU 727841	B2	20010104		
EP 986558	A2	20000322	EP 1998-932090	19980527
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
BR 9809491	A	20001017	BR 1998-9491	19980527
JP 2001527580	T2	20011225	JP 1999-500237	19980527
CZ 289466	B6	20020116	CZ 1999-4245	19980527
ZA 9804560	A	19981130	ZA 1998-4560	19980528
NO 9905482	A	19991109	NO 1999-5482	19991109
US 6221870	B1	20010424	US 1999-424377	19991123
PRIORITY APPLN. INFO.: GB 1997-11043 A 19970529				
WO 1998-EP3125 W 19980527				
OTHER SOURCE(S): MARPAT 130:25220				
GI				



AB Ergoline derivs. I [R1 = H, alkyl; R2 = H, halogen, alkyl; R3 = H, alkyl; R4 = substituted Ph, pyridinyl, 2,1,3-benzoxadiazolyl, benzo[1,2-c:3,4-c']bis[1,2,5]oxadiazolyl; R5 = R6 = H; R5R6 = **bond**] were prepd. for use and somatosatin receptor antagonists (no data) for possible treatment of depression, anxiety, bipolar disorders, and ADHD. Thus, ergoline II was prepd. via amidation of 2-bromo-9,10-dihydrolysergic acid with 1-methyl-6-(1-piperazinyl)-2(1H)-pyridinone,.

L65 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:649288 HCAPLUS

DOCUMENT NUMBER: 130:2266

TITLE: Solubilization and pharmacological characterization of a glucocorticoid membrane receptor from an amphibian brain

AUTHOR(S): Evans, Simon J.; Moore, Frank L.; Murray, Thomas F.

CORPORATE SOURCE: Molecular and Cellular Biology Program, Oregon State University, Corvallis, OR, 97331, USA

SOURCE: Journal of Steroid Biochemistry and Molecular Biology (1998), 67(1), 1-8

CODEN: JSBBEZ; ISSN: 0960-0760

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Physiol. functions of **steroid** hormones involve activation of intracellular **receptors** as well as poorly understood membrane receptors. The authors report the pharmacol. characterization of a solubilized corticosterone receptor from neuronal membranes. This receptor previously was shown to localize with plasma membrane subcellular fractions and to be involved in the modulation of courtship behaviors in the roughskin newt (*Taricha granulosa*). The authors describe procedures with non-ionic detergents that solubilize the receptor and maintain high affinity [<sup>3</sup>H]corticosterone binding. The pharmacol. of the solubilized corticosterone receptor resembles that of the membrane receptor with high affinity for [<sup>3</sup>H]corticosterone and an identical rank-order potency for other steroid ligands (corticosterone>cortisol>aldosterone>dexamethasone). Unlike binding in membrane preps., [<sup>3</sup>H]corticosterone binding to the solubilized receptor is insensitive to neg. modulation by guanyl nucleotides and only modestly sensitive to the presence of Mg<sup>2+</sup>. The authors also identified two ligands that exhibit high affinity binding to

the solubilized receptor and have the potential to be used in an affinity purifn. scheme. They are corticosterone-3-carboxymethyloxime (CORT-3-CMO), which may be covalently attached to a Sepharose resin, and a derivitized azide form of CORT-3-CMO which can be covalently coupled to the solubilized receptor itself. The stability of the solubilized [3H]corticosterone receptor in the detergent system will facilitate further purifn. and mol. characterization.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:192313 HCAPLUS

DOCUMENT NUMBER: 120:192313

TITLE: Preparation of dehydrophenylalanine-containing peptides as bombesin agonists or antagonists.

INVENTOR(S): Edwards, Judson V.; Fanger, Bradford O.

PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 54 pp.

CODEN: PIXXD2

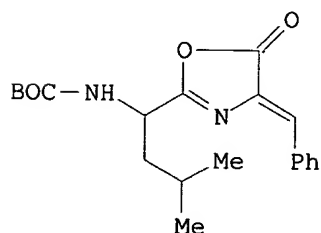
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316105	A1	19930819	WO 1993-US183	19930107
W: AU, CA, FI, HU, JP, KR, NO, NZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9334399	A1	19930903	AU 1993-34399	19930107
AU 668909	B2	19960523		
EP 626973	A1	19941207	EP 1993-903045	19930107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07505865	T2	19950629	JP 1993-513250	19930107
HU 71585	A2	19951228	HU 1994-2285	19930107
ZA 9300716	A	19930901	ZA 1993-716	19930202
US 5428018	A	19950627	US 1994-263905	19940622
FI 9403638	A	19940805	FI 1994-3638	19940805
NO 9402919	A	19940805	NO 1994-2919	19940805
PRIORITY APPLN. INFO.:			US 1992-833834	19920207
			WO 1993-US183	19930107
OTHER SOURCE(S):			MARPAT 120:192313	
GI				



AB H-Glp-Gln-Trp-Ala-Val-Gly-A1-Q-A2-Y and X-A3-Q-A4-Gln-Trp-Ala-Val-Gly-His-Leu-Y [A1 = His, Leu, His-Leu, bond; A2 = Phe, Leu, Phe-Leu, bond; A3 = Glp, bond; A4 = Gly, bond; Q =

modified Phe; X = H, 1-2 alkyl, 1-2 acyl, Z, BOC, null; Y = OH, alkoxy ester, carboxamide, mono- or dialkylamine, thioalkyl ether], were prepd. Thus, tert-butoxycarbonylleucyl-DL-phenylserine (prepn. given) was stirred with NaOAc in HOAc to give 90% BOC-Leu-.DELTA.zPhe azlactone (I). I was stirred with dimethylaminopyridine in MeOH to give BOC-Leu-.DELTA.zPhe-OMe, which was deprotected and coupled with Ac-D-Phe-Gln-Trp-Ala-Val-Gly-His-OH in DMF using diisopropylamine/diphenylphosphoryl azide to give Ac-D-Phe-Gln-Trp-Ala-Val-Gly-His-Leu-.DELTA.zPhe-OMe. This bound to mouse pancreas **bombesin receptors** with  $K_d = 1.18$  nM, showing antagonist/partial agonist activity.

L65 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:154319 HCAPLUS

DOCUMENT NUMBER: 120:154319

TITLE: Bombesin receptors in a human duodenal tumor cell

line: binding properties and function

AUTHOR(S): Williams, Barbara Y.; Schonbrunn, Agnes

CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77225, USA

SOURCE: Cancer Res. (1994), 54(3), 818-24

CODEN: CNREA8; ISSN: 0008-5472

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The bombesin family of peptides elicit numerous biol. responses in the gut, including stimulation of cell proliferation, and have been implicated as growth factors in a variety of gastrointestinal tumors. Even though these peptides and their receptors are distributed throughout the gastrointestinal tract, there are few cell lines available as model systems to study bombesin action in gastrointestinal cells. In this study, the authors have characterized functional **bombesin receptors** in a human duodenal cancer cell line, HuTu-80. The binding of [125I-Tyr4]bombesin to intact cells at 4.degree. reached equil. by 6 h. Scatchard anal. of [125I-Tyr4]bombesin binding showed that HuTu-80 cells contained a single class of high affinity binding sites (5900/cell;  $K_d = 80$  pM). [125I-Tyr4]**bombesin** binding was inhibited by **bombesin receptor** agonists and antagonists with the following order of potencies: gastrin-releasing peptide (GRP) = GRP-(14-27) = bombesin > [D-Phe6]bombesin(6-13)ethylamide > [Leu13.psi.(CH2NH)Leu14]bombesin > neuromedin B. Photoaffinity crosslinking studies, in which N-5-azido-2-nitrobenzoyloxysuccinimide was used to **covalently** couple [125I]GRP(14-27) to cells at 4.degree., resulted in the specific labeling of a broad band with an apparent mol. mass of 66,000 Da. Consistent with the presence of high affinity **receptors, bombesin** increased the formation of inositol phosphates in HuTu-80 cells in a dose-dependent manner (concn. eliciting half-maximal effect, 290 pM). However, under conditions where both insulin and serum increased [3H]thymidine incorporation into DNA, 10 nM bombesin had no effect either alone or in the presence of insulin. Bombesin also had no effect on colony formation by HuTu-80 cells in soft sugar. Furthermore, the **bombesin receptor** antagonist, [Leu13.psi.(CH2NH)Leu14]**bombesin**, did not inhibit [3H]thymidine incorporation or clonal growth either in the absence or in the presence of serum. Together, these results show that HuTu-80 cells contain high affinity **bombesin receptors** of the GRP subtype. These receptors are functionally coupled to second messenger prodn. but do not stimulate cell proliferation.

L65 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:16493 HCAPLUS

DOCUMENT NUMBER: 118:16493  
 TITLE: The **covalent** labeling of proteins by 17.beta.-estradiol, retinoic acid, and progesterone in the human breast cancer cell lines MCF-7 and MCF-7/AdrR  
 AUTHOR(S): Takahashi, Noriko; Breitman, Theodore R.  
 CORPORATE SOURCE: Div. Cancer Treat., Natl. Cancer Inst., Bethesda, MD, 20892, USA  
 SOURCE: J. Steroid Biochem. Mol. Biol. (1992), 43(6), 489-97  
 CODEN: JSBBEZ; ISSN: 0960-0760  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The **covalent** bindings to proteins of 17.beta.-estradiol (E2), retinoic acid (RA), and progesterone in MCF-7 and MCF-7/AdrR cells were studied. MCF-7 cells have receptors for E2 and progesterone; MCF-7/AdrR cells do not have these receptors. After a 1-day incubation period with either [3H]E2, [3H]progesterone, or [3H]RA, the levels of **covalently** bound radioactivity were 1.4-2-fold greater in MCF-7 cells than in MCF-7/AdrR cells. The labeled proteins were analyzed with 2-dimensional PAGE and fluorog. About 40 proteins were labeled by E2 in MCF-7 cells and about 10 of these proteins were the only proteins labeled by E2 in MCF-7/AdrR cells. The same 8 proteins were labeled by RA in both cell lines. Progesterone labeled 2 proteins with Mr values of 37,000 and 20,000 in MCF-7 cells. These 2 proteins had mobilities that were the same as proteins that were labeled by either E2 or RA in both MCF-7 and MCF-7/AdrR cells. Besides these 2 proteins, proteins of Mr 51,000 (p51) and 55,000 were **covalently** labeled by E2 in MCF-7 cells and by RA in both MCF-7 and MCF-7/AdrR cells. The p51 had the same mobility on 2-dimensional PAGE as an 8-azido-[32P]cAMP-labeled protein. This protein is probably RII.alpha., the type II cAMP-binding regulatory subunit of type II cAMP-dependent protein kinase. Thus, the estrogen receptor, while not obligatory, might still modulate the **covalent linkage** of E2 to protein. In addn., it is possible that some effects of some ligands of the thyroid/steroid hormone **receptor** family may involve the **covalent linking** of these hormones to proteins, including RII.alpha..

L65 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1991:97019 HCAPLUS  
 DOCUMENT NUMBER: 114:97019  
 TITLE: Purification and N-terminal amino acid sequence of the Ah receptor from the C57BL/6J mouse  
 AUTHOR(S): Bradfield, Christopher A.; Glover, Edward; Poland, Alan  
 CORPORATE SOURCE: Med. Sch., Univ. Wisconsin, Madison, WI, 53706, USA  
 SOURCE: Mol. Pharmacol. (1991), 39(1), 13-19  
 CODEN: MOPMA3; ISSN: 0026-895X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The Ah receptor is a presumed member of the superfamily of **steroid** /thyroid hormone **receptors**. This protein was purified to homogeneity (from the liver of C57BL/6J mice) and its N-terminal amino acid sequence was detd. Selective **covalent** labeling of the Ah receptor in hepatic cytosol with the photoaffinity ligands 2-azido-3-[125I]iodo-7,8-dibromodibenzo-p-dioxin simplified identification and quantitation of the receptor and permitted purifn. under denaturing conditions. Photoaffinity-labeled hepatic cytosol was applied to a phosphocellulose column at 80 mM NaCl, and the fraction enriched with the Ah receptor eluted with 225 mM NaCl. The eluate was dild. to 150 mM NaCl and applied to a DEAE-cellulose column, and the enriched fraction eluted

with 300 mM. These two ion exchange chromatog. steps usually gave .apprx.100-fold enrichment and 40-50% recovery of Ah receptor. The dil. protein in the eluate was pptd. with n-propanol/trichloroacetic acid and solubilized in formic acid. The sample was then subjected to 3 successive rounds of HPLC on C4 reverse phase columns. The final, shallow-gradient chromatog. was able to resolve the unlabeled 95-kDa receptor protein from the later eluting 125I-photoaffinity-labeled protein. The pooled HPLC fractions subjected to electrophoresis on SDS-polyacrylamide gels contained only the 95-kDa band upon staining with Coomassie blue R250 or silver. Using the above protocol, the Ah receptor was purified >150,000-fold, to apparent homogeneity, with an overall yield of 3-5%. The N-terminal amino acid sequence of the purified peptide was detd. to be ala/asp-ser-Arg-Lys-arg-Lys-Pro-Val-Gln-Lys-Thr-Val-Lys-Pro-Lle-Pro-Ala-Glu-Gly--Ile-Lys-ser-Asn-Pro-ser-Lys- (where the lowercase indicates a residue detd. with less confidence).

L65 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:36140 HCAPLUS

DOCUMENT NUMBER: 114:36140

TITLE: Structural characterization of the somatostatin receptors on rat cerebrocortical membranes. II. Studies on receptor structure using cross-linking method

AUTHOR(S): Nagao, Munehiko; Sakamoto, Choitsu; Matozaki, Takashi; Nishizaki, Hogara; Konda, Yoshitaka; Nakano, Osamu; Baba, Shigeaki

CORPORATE SOURCE: Sch. Med., Kobe Univ., Kobe, 650, Japan

SOURCE: Nippon Naibunpi Gakkai Zasshi (1990), 66(10), 1108-16

CODEN: NNGZAZ; ISSN: 0029-0661

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB Crosslinking of 125I-labeled [Tyr1]-**somatostatin** to its **receptor** on rat cerebrocortical and pancreatic acinar cell membranes occurred to reveal 72,000 and 92,000 bands, resp., when N-5-azido-nitrobenzoyloxysuccinimide (ANB-NOS) was employed as a cross-linker. Crosslinking N-hydroxysuccinimidyl-4-**azidobenzonate** (HSAB), sulfosuccinimidyl-2-(p-**azidosalicylamide**)ethyl-1,3-dithiopropionate, or disuccinimidylsuberate (DSS) did not work as well. The binding of **somatostatin** to the crosslinked-**receptor** with diminished in the presence of Gpp(NH)p, a non-hydrolyzed deriv. of guanine nucleotide, or by prior treatment with islet activating protein (IAP). The receptor of cerebrocortical membrane was solubilized with Zwittergent 3-12, and bound to wheat germ agglutinin. The lectin binding was inhibited by N,N',N''-triacetylchitotriose or N-acetylglucosamine. Thus, **somatostatin receptors** on cerebrocortical membranes are a monomeric glycoprotein with a Mr = 70,000 contg. no disulfide-linked binding subunit, which is coupled to islet activating protein-sensitive guanine nucleotide regulatory protein.

L65 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:673 HCAPLUS

DOCUMENT NUMBER: 114:673

TITLE: Des-Met carboxyl-terminally modified analogs of bombesin function as potent bombesin receptor antagonists, partial agonists, or agonists

AUTHOR(S): Wang, Lu Hua; Coy, David H.; Taylor, John E.; Jiang, Ning Yi; Moreau, Jacques Pierre; Huang, Shih Che; Frucht, Harold; Haffar, Bassam M.; Jensen, Robert T.

CORPORATE SOURCE: Dig. Branch, Natl. Inst. Diabetes Dig. Kidney Dis.,



SOURCE: Bethesda, MD, 20892, USA  
 J. Biol. Chem. (1990), 265(26), 15695-703  
 CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effect of carboxyl-terminal modifications of des-Met14-**bombesin** (Bn) on Bn **receptor** affinity in murine 3T3 cells, rat and guinea pig pancreatic acini, and the ability to initiate biol. responses were examd. by synthesizing 18 des-Met14-Bn(6-13) analogs. With guinea pig acini and cells, affinity was affected by the chain lengths of the alkyl moiety (R) added to [D-Phe6]Bn(6-13)NH<sub>2</sub>R with relative potencies: Pr > Et > Bu = hexyl > heptyl > free amide, whereas in rat acini affinity was not increased by the chain length. In each cell system the affinity of the alkylamide was not increased by insertion of a Ph group in the alkyl side chain, by making the analog more neuromedin B-like, or by addn. of a reduced peptide **bond**. The affinity in each cell system was increased by addns. of other electron releasing groups to the COOH-terminal carboxyl group such as [D-Phe6]Bn(6-13)ethyl or Me ester, or **hydrazide**. In guinea pig pancreas and 3T3 cells, 12 analogs were antagonists, 1 a full and 5 partial agonists. In rat pancreas, 8 were antagonists, 5 full agonists, and 5 partial agonists. Potent antagonists in each cell system were the Me and Et ester, **hydrazide**, and ethylamide analogs. In 3T3 cells or guinea pig pancreas, agonist activity of the alkylamide was critically dependent on the chain length, whereas with rat pancreatic Bn receptors any alkylamide longer than the ethylamide had agonist activity. In all 3 cell systems any alteration that made the alkylamide more neuromedin B-like caused agonist activity. Thus, the nature of the substitution on the carboxyl terminus of des-Met14-Bn analog is critically important, not only for detg. Bn receptor affinity, but also for detg. the ability to initiate a biol. response. Evidently, the presence of the COOH-terminal amino acid in position 14 of Bn is not essential for initiating a biol. response. Several des-Met14-Bn analogs were potent partial agonists, whereas others such as the **hydrazide** or Et ester are very potent antagonists.

L65 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:650 HCAPLUS

DOCUMENT NUMBER: 114:650

TITLE: Identification of somatostatin receptors by **covalent** labeling with a novel photoreactive somatostatin analog

AUTHOR(S): Brown, Patricia J.; Lee, Angie B.; Norman, Marjorie G.; Presky, David H.; Schonbrunn, Agnes

CORPORATE SOURCE: Med. Sch., Univ. Texas, Houston, TX, 77225, USA

SOURCE: J. Biol. Chem. (1990), 265(29), 17995-18004

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two photoreactive derivs. of somatostatin, namely 125I-labeled [Tyr11, **azidonitrobenzoyl**-Lys4]somatostatin ([125I-Tyr11,ANB-Lys4]somatostatin) and [125I-Tyr11,ANB-Lys9]somatostatin were synthesized and used to characterize **somatostatin receptors** biochem. in several cell types. Satn. binding expts. carried out in the dark demonstrated that [125I-Tyr11,ANB-Lys4]somatostatin bound with high affinity (K<sub>d</sub> = 126 pM) to a single class of binding sites in GH4C1 pituitary cell membranes. The affinity of this analog was similar to that of the unsubstituted peptide [125I-Tyr11]somatostatin (207 pM). In contrast, specific binding was not obsd. with [125I-Tyr11,ANB-Lys9]somatostatin. The binding of both [125I-Tyr11,ANB-Lys4]somatostatin and [125I-Tyr11]somatostatin was potently inhibited by somatostatin (EC50

= 300 pM), whereas unrelated peptides at 100 nM had no effect. Furthermore, both pertussis toxin treatment and guanyl-5'-yl imidophosphate (Gpp(NH)p) markedly reduced [125I-Tyr11,ANB-Lys4]somatostatin binding. Thus, [125I-Tyr11,ANB-Lys4]somatostatin binds to G protein-coupled **somatostatin receptors** with high affinity. To characterize these receptors biochem., GH4C1 cell membranes were irradiated with UV light following the binding incubation, and the labeled proteins were identified by SDS-PAGE and autoradiog. A major band of 85 kDa was specifically labeled with [125I-Tyr11,ANB-Lys4]somatostatin but not with [125I-Tyr11,ANB-Lys9]somatostatin or [125I-Tyr11]somatostatin. The binding affinity of the 85-kDa protein for [125I-Tyr11,ANB-Lys4]somatostatin was very high ( $K_d = 34$  pM). Labeling of this protein was inhibited competitively by somatostatin ( $EC_{50} = 140$  pM) but not by unrelated peptides. Furthermore, this band was not labeled in pertussis toxin-treated membranes or in untreated membranes incubated with Gpp(NH)p. Finally, [125I-Tyr11,ANB-Lys4]somatostatin specifically labeled bands of 82, 75, and 72 kDa in membranes prep'd. from mouse pituitary AtT-20 cells, rat pancreatic acinar AR4-2J cells, and HIT hamster islet cells, resp. Thus, [125I-Tyr11,ANB-Lys4]somatostatin represents the first photolabile **somatostatin** analog able to bind to **receptors** with high affinity. This novel peptide **covalently** labels specific **somatostatin receptors** in a variety of target cell types.

L65 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1989:527365 HCAPLUS  
 DOCUMENT NUMBER: 111:127365  
 TITLE: Biochemical properties of brain somatostatin receptors  
 AUTHOR(S): Thermos, K.; He, H. T.; Wang, H. L.; Margolis, N.;  
 Reisine, T.  
 CORPORATE SOURCE: Sch. Med., Univ. Pennsylvania, Philadelphia, PA,  
 19104, USA  
 SOURCE: Neuroscience (Oxford) (1989), 31(1), 131-41  
 CODEN: NRSCDN; ISSN: 0306-4522  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The phys. properties of brain and pituitary **somatostatin receptors** were characterized using photocrosslinking techniques. **Somatostatin receptors** in rat corpus striatum and anterior pituitary membranes were **covalently** bound to the non-reducible somatostatin analog, [125I]CGP 23996, using the crosslinking agent N-hydroxysuccinimidyl-4-**azidobenzoate** and UV light. In striatal membranes, a protein of 60,000 mol. wt. was labeled by [125I]CGP 23996. The binding was potently inhibited by somatostatin analogs but not by other biol. active peptides. The labeling of the 60,000-mol.-wt. protein by [125I]CGP 23996 was diminished by guanine triphosphate gamma thiol, which is consistent with the labeling of a **somatostatin receptor** coupled to GTP binding proteins. The migration of the [125I]CGP 23996 labeled 60,000-mol.-wt. protein in native SDS-gels was not affected by the reducing agent dithiothreitol, indicating that there is a general lack of disulfide bridges in the striatal **somatostatin receptor**. The striatal **somatostatin receptor** was solubilized with the detergent 3-[(3-cholamidopropyl)-dimethylaminoio]-1-propanesulfonate and specifically bound to the lectin wheat germ agglutinin, suggesting that the striatal **somatostatin receptor** is a glycoprotein. [125I]CGP 23996 also labeled a 60,000-mol.-wt. protein in anterior pituitary membranes. The characteristics of [125I]CGP 23996 binding to anterior pituitary membranes were consistent with the labeling of a **somatostatin receptor**. Interestingly, a comparison of the [125I]CGP 23996

labeled material from striatal and anterior pituitary membranes by 2-dimensional PAGE revealed the presence of several striatal **somatostatin receptors** of varying charge (pI values between 6 and 6.5) but only a single pituitary receptor. Phys. differences may thus exist between subtypes of **somatostatin receptors**.

L65 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1989:417963 HCAPLUS

DOCUMENT NUMBER: 111:17963

TITLE: Characterization of 17.beta.-estradiol-dependent and -independent somatostatin receptor subtypes in rat anterior pituitary

AUTHOR(S): Kimura, Nobuko; Hayafuji, Chieko; Kimura, Narimichi

CORPORATE SOURCE: Dep. Mol. Neurobiol., Tokyo Metrop. Inst. Neurosci., Fuchu, 183, Japan

SOURCE: J. Biol. Chem. (1989), 264(12), 7033-40

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Both the estradiol (E2)-dependent and E2-independent **somatostatin** (SRIF) **receptors**, measured with 125I-labeled Tyr11-SRIF as a radiolabeled ligand, were enriched in the plasma membrane fraction of anterior pituitary cells, each displaying a single class of binding site (E2-dependent: Kd, 32 pM and Bmax, 2.3 pmol/mg protein; E2-independent: Kd, 83 pM and Bmax, 0.26 pmol/mg protein) in ovariectomized rats. The ligand binding to both receptors was sensitive to monovalent and divalent cations and to GTP. Among the SRIF analogs tested, the relative potencies of SRIF28, an analog, and cyclosomatostatin compared with SRIF were lower in the E2-dependent receptor than in the E2-independent one. A crosslinking study with N-hydroxysuccinimidyl-4-**azidobenzoate** revealed that the mol. wt. of the cross-linked E2-dependent receptor was approx. 94,000, whereas that of the E2-independent one was 82,000, irrespectively of the presence of a reducing reagent. The mol. wt. of SRIF receptor from normal male or female rat pituitary was similar to the E2-independent type. Both types of the cross-linked SRIF receptors were solubilized by sucrose monolaurate, adsorbed to a wheat germ agglutinin-agarose column, and eluted with N-acetyl-glucosamine. SRIF inhibited the forskolin-stimulated adenylate cyclase activity in the pituitary membranes from E2-treated rats, but it did not in the E2-depleted membranes. Thus, there are at least 2 subtypes of SRIF receptor in the rat pituitary anterior pituitary, one of which is exclusively expressed by treatment with E2. and these subtypes are distinct with respect to ligand binding specificity, mol. wt., and coupling to adenylate cyclase inhibition.

L65 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1989:128862 HCAPLUS

DOCUMENT NUMBER: 110:128862

TITLE: **Covalent** labeling of the somatostatin receptor in rat anterior pituitary membranes

AUTHOR(S): Bruno, John F.; Berelowitz, Michael

CORPORATE SOURCE: Dep. Med., State Univ. New York, Stony Brook, NY, 11794, USA

SOURCE: Endocrinology (Baltimore) (1989), 124(2), 831-7

CODEN: ENDOAO; ISSN: 0013-7227

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The mol. characteristics of the **somatostatin** (SRIF) **receptor** were investigated by **covalently** crosslinking

[125I-Tyr11]SRIF to rat anterior pituitary membranes using 3 heterobifunctional crosslinking agents, N-5-azido-2-nitrobenzoyloxysuccinimide, N-hydroxysuccinimidyl-4-azidobenzoate, and N-succinimidyl-6-(4'-azido-2'-nitrophenylamino) hexanoate, and the homobifunctional agent disuccinimidyl suberate. SDS-gel electrophoresis followed by autoradiog. revealed 2 SRIF-binding proteins with apparent mol. wt. (Mr) and 69,000 and 66,000 that were selectively labeled by the 4 crosslinking agents. When crosslinking was performed with N-5-azido-2-nitrobenzoyloxysuccinimide, both proteins migrated as a broad band centered at 68,000; however, with N-hydroxysuccinimidyl-4-azidobenzoate, the band was resolved into 69,000- and 66,000-Mr components. N-Succinimidyl-6-(4'-azido-2'-nitrophenylamino) hexanoate covalently labeled the 69,000-Mr protein and a minor species with a Mr of 45,000-47,000. Crosslinking with disuccinimidyl suberate labeled only the 66,000 Mr band. Labeling of both bands was specific, since affinity labeling with each of the 4 agents was abolished when 1 .mu.M cyclic SRIF was included in the binding reaction. Binding of [125I-Tyr11]SRIF to membranes and labeling of the 69,000 and 66,000 Mr SRIF-binding species were similarly inhibited in a dose-dependent manner by unlabeled SRIF. Radiolabeling of both proteins was specifically displaced by 1 .mu.M SRIF-28 and [D-Trp8,D-Cys14]SRIF, but not by oxytocin. Moreover, the extent of radiolabel incorporation into both components was dependent of the concn. of [125I-Tyr11]SRIF in the binding reaction. These results demonstrate the presence of 2 SRIF-binding proteins in rat anterior pituitary membranes that show characteristics of the SRIF receptor.

L65 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1988:583805 HCAPLUS

DOCUMENT NUMBER: 109:183805

TITLE: Somatostatin receptors on rat cerebrocortical membranes. Structural characterization of somatostatin-14 and somatostatin-28 receptors and comparison with pancreatic type receptors

AUTHOR(S): Sakamoto, Choitsu; Nagao, Munehiko; Matozaki, Takashi; Nishizaki, Hogara; Konda, Yoshitaka; Baba, Shigeaki

CORPORATE SOURCE: Sch. Med., Kobe Univ., Kobe, 650, Japan

SOURCE: J. Biol. Chem. (1988), 263(28), 14441-5

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Somatostatin** binding and crosslinking to its **receptors** on rat cerebrocortical membranes were characterized with 125I-labeled [Tyr1]somatostatin-14 and 125I-labeled [Leu8,D-Trp22,Tyr25]somatostatin-28. When 125I-labeled [Tyr1]somatostatin-14 was cross-linked to its receptors with the photoreactive cross-linker, N-(5-azido-2-nitrobenzoyloxy)succinimide, the hormone was specifically assocd. with a Mr = 72,000 protein band in the presence or absence of reducing agents. Affinity labeling of the Mr = 72,000 protein band was decreased with increasing concns. of unlabeled somatostatin-14 and nonhydrolyzable guanine nucleotide analog, guanylyl-5'-yl imidodiphosphate (Gpp(NH)p). Pretreatment of cerebrocortical membranes with islet-activating protein resulted in a decrease in subsequent labeled somatostatin-14 binding and affinity labeling of the protein and abolished an inhibitory effect of somatostatin-14 on VIP-stimulated increase in adenylate cyclase activity. When the affinity-labeled protein was solubilized with Zwittergent 3-12 and adsorbed to wheat germ agglutinin-agarose, it was eluted by N-acetylglucosamine. 125I-labeled [Leu8,D-Trp22, Tyr25]somatostatin-28 crosslinking to cerebrocortical and

pancreatic membranes with the same photoreactive agent revealed specifically labeled protein bands of a 94,000 in pancreatic membranes, resp. Thus, **somatostatin receptor** on cerebrocortical membranes is a monomeric glycoprotein with a Mr = 70,000 binding subunit, coupled to guanine nucleotide regulatory protein. The Mr = 70,000 protein may be a common **receptor** for **somatostatin-28** and **somatostatin-14** and is distinct from a common pancreatic type receptor.

L65 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1988:542912 HCAPLUS

DOCUMENT NUMBER: 109:142912

TITLE: Molecular characterization of the solubilized receptor of somatostatin from rat pancreatic acinar membranes

AUTHOR(S): Knuhtsen, Svend; Esteve, Jean Pierre; Bernadet, Brigitte; Vaysse, Nicole; Susini, Christiane

CORPORATE SOURCE: Groupe Rech. Biol. Pathol. Dig., CHU Rangueil, Toulouse, 31054, Fr.

SOURCE: Biochem. J. (1988), 254(3), 641-7

CODEN: BIJOAK; ISSN: 0306-3275

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The **somatostatin receptors** on rat pancreatic acinar membranes were demonstrated by use of a radioiodinated analog of somatostatin (SMS 204-090 or [Tyr3]SMS). The tracer bound to the receptor with a Kd of 58 pM. The no. of sites detected by this tracer (4.7 pmol/mg of protein) was 5-10 times higher than the no. of sites previously found with other tracers. Since the level of nonspecific binding was also very low as compared with findings with other tracers, 125I-labeled 204-090 might be of interest in future attempts to characterize the **somatostatin receptors** in the pancreas. The prelabeled membranes were solubilized with 1% CHAPS, and the solubilized complexes adsorbed to wheat germ agglutinin-coupled agarose, from which they could be eluted with 4 mM triacetylchitotriose. The complexes within this eluate were shown by gel filtration on Trisacryl GF-2000 to have an Mr of about 400,000. The dissociation of the complexes was augmented both within the membranes as well as in the solubilized state by incubation with the GTP analog guanosine 5'-[gamma-thio]triphosphate, indicating that the complexes are probably functionally **linked** to a guanine nucleotide-binding regulatory protein. After SDS/slab-gel electrophoresis and autoradiography of cross-linked complexes after treatment with the heterobifunctional reagent N-5-azido-2-nitrobenzoyloxysuccinimide, a broad band occurred at approx. Mr 90,000 both in the membranes and in the eluates of complexes after lectin-adsorption chromatography. Thus, the augmentation of the no. of detectable sites for binding of somatostatin, as well as the very low level of nonspecific binding obtained by the use of 125I-labeled [Tyr3]SMS as tracer, has made it possible to demonstrate the solubilization of the **somatostatin receptor** in conjunction with its ligand and a GTP-binding regulatory protein. Crosslinking of the 125I-labeled [Tyr3]SMS to a binding subunit of Mr 90,000 in the membranes was demonstrated and the presence of the same labeled binding subunit within complexes solubilized and chromatographed on a lectin column before crosslinking was also shown.

L65 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1988:522810 HCAPLUS

DOCUMENT NUMBER: 109:122810

TITLE: Pertussis toxin modifies the characteristics of both the inhibitory GTP binding proteins and the somatostatin receptor in anterior pituitary tumor

cells  
 AUTHOR(S): Mahy, Nicole; Woolkalis, Marilyn; Thermos, Kyriaki;  
 CORPORATE SOURCE: Carlson, Kenneth; Manning, David; Reisine, Terry  
 Sch. Med., Univ. Pennsylvania, Philadelphia, PA,  
 19104, USA  
 SOURCE: J. Pharmacol. Exp. Ther. (1988), 246(2), 779-85  
 CODEN: JPETAB; ISSN: 0022-3565  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The effects of pertussis toxin treatment on the characteristics of **somatostatin receptors** in the anterior pituitary tumor cell line AtT-20 were examd. Pertussis toxin selectively catalyzed the ADP ribosylation of the .alpha.-subunits of the inhibitory GTP binding proteins in AtT-20 cells. Toxin treatment abolished somatostatin inhibition of forskolin-stimulated adenylyl cyclase activity and somatostatin stimulation of GTPase activity. To examine the effects of pertussis toxin treatment on the characteristics of the **somatostatin receptor**, the **receptor** was labeled by the 125I-labeled somatostatin analog CGP 23996 ([125I]CGP 23996): [125I]CGP 23996 binding to AtT-20 cell membranes was saturable and within a limited concn. range was to a single high-affinity site. Pertussis toxin treatment reduced the apparent d. of the high-affinity [125I]CGP 23996 binding sites in AtT-20 cell membranes. Inhibition of [125I]CGP 23996 binding by a wide concn. range of CGP 23996 revealed the presence of 2 binding sites. GTP predominantly reduced the level of high-affinity sites in control membranes. Pertussis toxin treatment also diminished the amt. of high-affinity sites. GTP did not affect [125I]CGP 23996 binding in the pertussis toxin-treated membranes. The high-affinity **somatostatin receptors** were covalently labeled with [125I]CGP 23996 and the photoactivated crosslinking agent n-hydroxysuccinimidyl-4-azidobenzoate. No high-affinity **somatostatin receptors**, covalently bound to [125I]CGP 23996, were detected in the pertussis toxin-treated membranes. This was consistent with pertussis toxin uncoupling the inhibitory G proteins from the **somatostatin receptor**, thereby converting the **receptor** from a mixed population of high- and low-affinity sites to only low-affinity receptors. However, attempts to reconstitute somatostatin's inhibition of forskolin-stimulated adenylyl cyclase activity with purified inhibitory GTP binding protein from rabbit liver were unsuccessful, suggesting, that pertussis toxin may induce other cellular effects besides its well established inactivation of the inhibitory G proteins.

L65 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1988:216581 HCAPLUS  
 DOCUMENT NUMBER: 108:216581  
 TITLE: Somatostatin receptor subtypes in the clonal anterior pituitary cell lines AtT-20 and GH3  
 AUTHOR(S): Thermos, Kyriaki; Reisine, Terry  
 CORPORATE SOURCE: Sch. Med., Univ. Pennsylvania, Philadelphia, PA,  
 19104, USA  
 SOURCE: Mol. Pharmacol. (1988), 33(4), 370-7  
 CODEN: MOPMA3; ISSN: 0026-895X  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The functional and biochem. characteristics of **somatostatin** (SRIF) **receptor** subtypes were examd. in the clonal pituitary cell lines AtT-20 and GH3. SRIF inhibits evoked Ca influx into each of these cell lines. The rank order of potencies of structural analogs of SRIF to inhibit Ca influx into GH3 vs. AtT-20 cells was different.

Inhibitory actions of SRIF on Ca influx desensitized in AtT-20 cells but not GH3 cells. The biochem. properties of the SRIF receptor subtypes in AtT-20 and GH3 cells were assessed by photoaffinity labeling of each receptor with the nonreducible SRIF analog [125I]CGP 23996 and the photocrosslinking agent N-hydroxysuccinimidyl-4-azidobenzoate. The **covalently** labeled receptors in both cell lines had the same size, 55 kilodaltons, as assessed by SDS-PAGE. The **covalent** binding of [125I]CGP-23996 to GH3 and AtT-20 cell membranes was blocked by 1 .mu.M SRIF, somatostatin 28, and Trp8-SRIF and was GTP sensitive. Anal. of the labeled receptors in GH3 and AtT-20 cell membranes by 2-dimensional PAGE indicated that they were of similar charge (pI = 6-6.5) and that they comigrate when applied together. Proteolysis of the GH3 and AtT-20 cell SRIF receptors with Staphylococcus aureus V-8 and thermolysin revealed similar peptide maps. Pretreatment of AtT-20 cells with different stable SRIF analogs abolished the subsequent equil. or **covalent** labeling of the SRIF receptor with [125I]CGP-23996. Similar treatment of GH3 cells did not reduce the **covalent** labeling of the SRIF receptor by [125I]CGP 23996. The functional characteristics of SRIF receptors in GH3 and AtT-20 cells are thus different. However, clear differences in the biochem. properties of these receptor subtypes were not obsd. Subtle variations in the structure of the SRIF receptors may therefore be responsible for the functional differences.

L65 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1987:492266 HCAPLUS  
 DOCUMENT NUMBER: 107:92266  
 TITLE: Structural characterization of the somatostatin receptor in rat anterior pituitary membranes  
 AUTHOR(S): Lewis, Laura Dunbar; Williams, John A.  
 CORPORATE SOURCE: Cell. Biol. Lab., Mt. Zion Hosp., San Francisco, CA, 94120, USA  
 SOURCE: Endocrinology (Baltimore) (1987), 121(2), 486-92  
 CODEN: ENDOAO; ISSN: 0013-7227  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB To structurally characterize the **somatostatin receptor** in the anterior pituitary, the chem. crosslinking reagent N-5-azido-nitrobenzoyloxysuccinimide was used to attach **covalently** [125I-Tyr11]**somatostatin-14** to its **receptor** in pituitary membranes. Rat anterior pituitary membranes were incubated with [125I-Tyr11]**somatostatin-14**, washed, and then treated with 100 .mu.M crosslinker, which was activated by exposure to UV light. Gel electrophoresis followed by autoradiog. revealed a broad band centered at 88,000 mol. wt. The appearance of this band was unaffected by dithiothreitol. Competitive inhibition of binding by unlabeled somatostatin resulted in a parallel inhibition of labeling of the 88,000-mol.-wt. protein. The addn. of guanine nucleotides in concns. that inhibit binding similarly inhibited crosslinking. The crosslinked membranes were solubilized in Zwittergent 3-12, a nondenaturing detergent, and the glycosylation pattern of the labeled protein was investigated by incubation with various lectins coupled to agarose. The crosslinked protein was selectively absorbed by wheat germ agglutinin, and this interaction was blocked by the addn. of N,N',N''-triacetylchitotriose, indicating that the rat anterior pituitary **somatostatin receptor** is a glycoprotein contg. polymer .beta.-1-4 **linked** N-acetylglucosamine groups. Apparently, the rat anterior pituitary **somatostatin receptor** is a glycoprotein of 88,000 mol. wt. contg. no disulfide-linked subunits.

L65 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1987:209762 HCAPLUS  
 DOCUMENT NUMBER: 106:209762  
 TITLE: Solubilization and characterization of guinea pig pancreatic somatostatin receptors  
 AUTHOR(S): Zeggari, Mustafa; Viguerie, Nathalie; Susini, Christiane; Garnier, Martine; Esteve, Jean Pierre; Ribet, Andre  
 CORPORATE SOURCE: Cent. Hosp. Univ. Rangueil, Toulouse, F-31054, Fr.  
 SOURCE: Eur. J. Biochem. (1987), 164(3), 667-73  
 CODEN: EJBCAI; ISSN: 0014-2956  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The solubilization of **somatostatin receptors** from guinea-pig pancreas by different nondenaturing detergents was investigated after stabilization of the receptors by prior binding of 125I-labeled [Tyr11]somatostatin or its analog 125I-labeled [Leu8,DTrp22,Tyr25]somatostatin 28, to pancreatic plasma membranes. The **somatostatin-receptor** complexes were solubilized in a high yield by Zwittergent 3-14 (3-[tetradecyldimethylammonio]-1-propanesulfonate), a zwitterionic detergent. Other detergents, digitonin, Triton X-100, Chaps (3-[cholamidopropyltrimethylammonio]-1-propanesulfonate) and octyl .beta.-D-glycopyranoside, achieved only partial solubilization. The recovery of receptor complexes was increased by glycerol. In order to characterize solubilized **somatostatin-receptor** complexes, membranes **receptors** were **covalently** labeled using N-5-azido-2-nitrobenzoyloxysuccinimide as crosslinking reagent before solubilization. Gel filtration chromatog. anal. resulted in the identification of a major protein component of apparent Mr (mol. wt.) 93,000 which interacted with the 2 radioligands. In addn., a similar component of Mr = 88,000 was characterized after anal. by SDS-PAGE of membrane receptors **covalently** crosslinked with 125I-labeled [Leu8,DTrp22,Tyr25]somatostatin 28 by different heterobifunctional reagents: N-5-azido-2-nitrobenzoyloxysuccinimide, N-hydroxysuccinimidyl 4-azidobenzoate, N-succinimidyl 6-(4'-azido-2'-nitrophenylamino)hexanoate. Optimal crosslinking results were obtained with N-5-azido-2-nitrobenzoyloxysuccinimide. The solubilized **somatostatin-receptor** complex was adsorbed to wheat-germ agglutinin-agarose column and eluted by specific sugars. Evidently, the guinea-pig pancreatic **somatostatin receptor** in the membrane and in the nondenaturing detergent soln. behaves as a protein monomer of apparent Mr .apprx.85,000-90,000. The **somatostatin receptor** is a glycoprotein which contains complex-type carbohydrate chains.

L65 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1987:29517 HCAPLUS  
 DOCUMENT NUMBER: 106:29517  
 TITLE: Photoaffinity labeling of neurotensin binding sites on rat brain sections  
 AUTHOR(S): Rostene, William H.; Mazella, Jean; Dussaillant, Monique; Vincent, Jean Pierre  
 CORPORATE SOURCE: Hop. Saint-Antoine, Paris, 75012, Fr.  
 SOURCE: Eur. J. Pharmacol. (1986), 130(3), 337-40  
 CODEN: EJPHAZ; ISSN: 0014-2999  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The photoaffinity labeling of neurotensin (NT)-binding sites was carried out in rat midbrain sections using a monoiodo analog of NT [125I-azidobenzoyl-NT (125IAB-NT)]. Autoradiog. data showed that the



125IAB-NT-binding site localization was quite similar to that obtained with 125I-labeled NT, with high densities in both substantia nigra and ventral tegmental area. **Covalent** specific binding was only obsd. when sections were irradiated with UV after the incubation, followed by various histol. treatments necessary for light and electron microscopy.

L65 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1986:605047 HCAPLUS

DOCUMENT NUMBER: 105:205047

TITLE: Characterization of **covalently** cross-linked pancreatic somatostatin receptors

AUTHOR(S): Susini, Christiane; Bailey, Anne; Szecowka, Jaroslaw; Williams, John A.

CORPORATE SOURCE: Med. Cent., Mount Zion Hosp., San Francisco, CA, 94120, USA

SOURCE: J. Biol. Chem. (1986), 261(35), 16738-43

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The **receptor** for **somatostatin** present in rat pancreatic plasma membranes was characterized by affinity labeling with [125I-labeled Tyr11]somatostatin utilizing 3 different heterobifunctional crosslinking agents: N-5-**azido**-2-nitrobenzoyloxy-succinimide, N-succinimidyl 6-(4-**azido** 2'-nitrophenylamine)hexanoate, and N-hydroxysuccinimidyl 4-**azido**-benzoate. Anal. by SDS-PAGE and autoradiog. revealed a broad band of mol. wt. (Mr) 92,000 when any of the 3 crosslinkers were used; N-succinimidyl 6-(4-**azido** 2'-nitrophenylamine), however, was most efficient. Labeling of the Mr 92,000 protein band was not affected by reducing agents but was sensitive to somatostatin and guanine nucleotides, particularly guanosine-5'-O-(thiotriphosphate), at concns. which reduced binding to the receptor. The affinity-labeled protein could be solubilized completely with Zwittergent 3-12, partially with Triton X-100 and 3-[(3-cholamidopropyl)dimethylammonio]-1-propanesulfonic acid, and poorly with Zwittergent 3-08 and digitonin. When exposed to agarose-coupled lectins, the detergent-solubilized, labeled Mr 92,000 protein was completely adsorbed to wheat germ agglutinin, partially to ricin communis II, and not at all to concanavalin A or lotus or lentil lectin. The Mr 92,000 protein bound to wheat germ agglutinin-agarose was not eluted by N-acetylglucosamine but was by triacetylchitotriose, providing a considerable purifn. of the **somatostatin receptor**. Evidently, the **somatostatin receptor** is a monomeric glycoprotein with an Mr 90,000 binding subunit which probably contains a polymeric arrangement of N-acetylglucosamine residues.

L65 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1986:142542 HCAPLUS

DOCUMENT NUMBER: 104:142542

TITLE: **Covalent** labeling of neurotensin receptors in rat gastric fundus plasma membranes

AUTHOR(S): Mazella, Jean; Kwan, Chiu Yin; Kitabgi, Patrick; Vincent, Jean Pierre

CORPORATE SOURCE: Cent. Biochim., Univ. Nice, Nice, 06034, Fr.

SOURCE: Peptides (Fayetteville, N. Y.) (1985), 6(6), 1137-41

CODEN: PPTDD5; ISSN: 0196-9781

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Neurotensin** [39379-15-2] **receptors** from plasma membranes of rat gastric fundus smooth muscle were specifically and **covalently** labeled by using the photoreactive analog 125I-labeled

**azidobenzoyl-(Trp11)-neurotensin** or by cross-linking monoiodo-Tyr3-neurotensin to the membrane prepn. by means of disuccinimidyl suberate. Anal. of plasma membranes by SDS-polyacrylamide gel electrophoresis and autoradiog. revealed that the same protein band with an apparent mol. wt. of 110,000 was specifically labeled by both methods. This band consisted of a single chain protein, since its apparent size was the same with or without redn. of membrane samples before electrophoresis. Only neurotensin and its biol. active analogs protected plasma membranes against specific labeling of the protein band of mol. wt. 110,000. Comparison of these results with those obtained from rat brain synaptic membranes showed that, although rat central and peripheral **neurotensin receptors** exhibit similar specificities towards a series of neurotensin analogs, their subunit structures are different.

L65 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1985:109304 HCAPLUS

DOCUMENT NUMBER: 102:109304

TITLE: Molecular properties of neurotensin receptors in rat brain. Identification of subunits by **covalent** labeling

AUTHOR(S): Mazella, Jean; Kitabgi, Patrick; Vincent, Jean Pierre  
CORPORATE SOURCE: Cent. Biochim., Univ. Nice, Nice, 06034, Fr.

SOURCE: J. Biol. Chem. (1985), 260(1), 508-14

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Neurotensin binding sites in rat brain synaptic membranes were specifically and **covalently** labeled by 2 methods. In the 1st, photoreactive and highly radioactive analog of neurotensin, 125I-labeled **azidobenzoyl[Trp11]neurotensin**, was synthesized and used to photoaffinity label **neurotensin receptors**. In the 2nd, the reversible assocn. between **neurotensin receptors** and 125I-labeled [Trp11]**neurotensin**, a radioactive but nonphotoreactive analog of neurotensin, was made irreversible by means of disuccinimidyl suberate, a bifunctional crosslinking reagent. Anal. of synaptic membranes by SDS-polyacrylamide gel electrophoresis and autoradiog. revealed that using both methods, the same 2 protein bands with apparent mol. wts. of 49,000 and 51,000 were specifically labeled. Identical results were obtained with or without redn. of the photolabeled membranes by .beta.-mercaptoethanol before electrophoresis. Variation of the ligand concn. did not modify the relative labeling intensities of the 2 bands, indicating that the high- and low-affinity neurotensin binding sites previously detected in rat brain synaptic membranes have similar mol. structures. Thus, **neurotensin receptors** in rat brain may be composed of 2 different protein subunits with similar mol. wt. of .apprx.50,000 that are **linked** together by noncovalent **bonds**.

L65 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1984:523556 HCAPLUS

DOCUMENT NUMBER: 101:123556

TITLE: The somatostatin receptor on isolated pancreatic acinar cell plasma membranes. Identification of subunit structure and direct regulation by cholecystokinin

AUTHOR(S): Sakamoto, Choitsu; Goldfine, Ira D.; Williams, John A.  
CORPORATE SOURCE: Cell Biol. Lab., Mt. Zion Hosp., San Francisco, CA, 94120, USA

SOURCE: J. Biol. Chem. (1984), 259(15), 9623-7

DOCUMENT TYPE:

CODEN: JBCHA3; ISSN: 0021-9258

LANGUAGE:

Journal

English

AB Cyclic **somatostatin** [38916-34-6] binding to its **receptors** on rat pancreatic acinar membranes was characterized with 125I-labeled tyrosine-somatostatin [59481-23-1]. Binding at 24.degree. was rapid, reaching a max. after 60 min and was reversible on the addn. of 1 .mu.Mm unlabeled ligand. Scatchard anal. revealed a single class of binding sites, with an apparent dissocn. const. of 0.32 nM and a binding capacity of 600 fmol/mg protein. Specificity for somatostatin was demonstrated with the inhibition of labeled hormone binding by somatostatin analogs in proportion to their biol. activities. When 125I-labeled tyrosine-somatostatin was crosslinked too its **receptors** with the photoreactive cross-linker n-hydroxysuccinimidyl-4-azidobenzoate, the hormone was assocd. with 90,000-mol.-wt. protein. Similar mobilities of the radioactive band were obsd. in the presence and absence of dithiothreitol. In contrast to other unrelated peptides, cholecystokinin (CCK) [9011-97-6] and its analogs directly reduced 125-labeled tyrosine-somatostatin binding to isolated membranes. The effect of CCK was half-maximal at 3 nM and maximal at 100 nM. In the presence of 3 nM cholecystokinin octapeptide [25126-32-3] (CCK8), the binding capacity for somatostatin was decreased to 237 fmol/mg protein without a significant change in affinity. Dibutyryl cGMP [32266-35-6], a CCK receptor antagonist, blocked this action of CCK8 indicating that the CCK receptor mediated the decrease in 125I-labeled tyrosine-somatostatin binding. In contrast cerebral cortex membranes, which also possess a **somatostatin receptor**, were not regulated by CCK. The binding of **somatostatin** to its **receptor** on pancreatic plasma membranes is apparently regulated by CCK analogs acting via the CCK receptor.

L65 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:

1980:54712 HCAPLUS

DOCUMENT NUMBER:

92:54712

TITLE:

Chemical compositions, their use as cytochemical agents and methods for the detection of steroid hormone receptors in human tissues

INVENTOR(S):

Lee, Sin Hang

PATENT ASSIGNEE(S):

USA

SOURCE:

Eur. Pat. Appl., 46 pp.

CODEN: EPXXDW

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 3583	A1	19790822	EP 1979-100329	19790205	
EP 3583	B1	19811202			
R: BE, CH, DE, FR, GB, IT, LU, NL, SE					
US 4215102	A	19800729	US 1979-1205	19790105	
PRIORITY APPLN. INFO.:				US 1978-876564	19780210
				US 1978-947700	19780929
				US 1979-1205	19790105

AB Novel chem. compns. are provided consisting essentially of a hormone-carrier-fluorochrome **conjugate**, esp. an estrogen-carrier-fluorochrome or a progesterone-carrier-fluorochrome **conjugate**. The **conjugates** are cytochem. agents and can be used in a method for the detection and identification of estrogen or

progesterone receptor cells in carcinomas of the breast by application of the agent to an excised unfixed frozen tissue section, which is then examd. for the appearance of fluorescent dye staining of the cells therein, for evaluation of potential endocrine or hormone therapy of the patient. Cytochem. agents and methods for the detection of other types of hormone receptor cells in various kinds of cancerous tissue are also disclosed, using sex hormones and endocrine steroid components.

L65 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1977:462922 HCAPLUS

DOCUMENT NUMBER: 87:62922

TITLE: Estrogen photoaffinity labels. 2. Reversible binding and **covalent** attachment of photosensitive hexestrol derivatives to the uterine estrogen receptor Katzenellenbogen, John A.; Carlson, Kathryn E.; Johnson, Howard J., Jr.; Myers, Harvey N.

CORPORATE SOURCE: Dep. Chem., Univ. Illinois, Urbana, Ill., USA

SOURCE: Biochemistry (1977), 16(9), 1970-6

CODEN: BICHAW

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The ability of 2 tritiated, photoreactive estrogen analogs, hexestrol diazoketopropyl ether ([<sup>3</sup>H]Hex-DKP) [63238-39-1] and hexestrol **azide** ([<sup>3</sup>H]Hex-N<sub>3</sub>) [63238-40-4], to **covalently** label the uterine estrogen receptor was studied. Lamb uterine estrogen receptor preps. that were partially purified (ammonium sulfate pptn., Sephadex G-200 chromatog.) and disaggregated by limited trypsinization can be electrophoresed on polyacrylamide gels under conditions where binding activity is preserved. This electrophoretic procedure was used to fractionate the proteins labeled by the 2 estrogen analogs. Prior to photolysis, peaks of radioactivity indicating estrogen specific binding of [<sup>3</sup>H]-Hex-N<sub>3</sub> and [<sup>3</sup>H]Hex-DKP are evident on the gels, although disocn. of the latter compd. is extensive. When preps. of uterine estrogen receptor that contain the photoreactive derivs. are irradiated and then electrophoresed, reversibly labeled proteins can be distinguished from irreversibly labeled ones (**covalently bonded**), by extn. of the individual gel slices with org. solvents. While no irreversible binding to receptor appears to result from irradiation with [<sup>3</sup>H]Hex-DKP, irradiation with [<sup>3</sup>H]Hex-N<sub>3</sub> does **covalently** label the estrogen receptor. The receptor **covalently** labeled with [<sup>3</sup>H]Hex-N<sub>3</sub> has the same electrophoretic mobility as the unlabeled receptor; the **covalent** labeling process is estrogen-site specific, and the efficiency of labeling (15-20%) is consistent with the inactivation efficiency of Hex-N<sub>3</sub>, previously measured by an indirect assay. This is the first example of the labeling of a **steroid hormone receptor** by photoaffinity labeling.

469 azide conjugated to cpd of cl. 2

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L15	24	SEA FILE=REGISTRY ABB=ON PLU=ON (AZIDE/CN OR "AZIDE (H(N3)21-)/CN OR "AZIDE (H(N3)21-), TETRAPHENYLPHOSPHONIUM"/CN OR "AZIDE (N3-)/CN OR "AZIDE DIBENZYLDMETHYLAMMONIUM"/CN OR "AZIDE ION"/CN OR "AZIDE ION(1-)/CN OR "AZIDE RADICAL"/CN OR "AZIDE(1-)/CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3-OOXOCTADECAXOCTADECANADATE(10-) (1:1)/CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3-OOXOCTADECAXOCTADECANADATE(13-) (1:1)/CN OR "AZIDE, LABELED WITH NITROGEN-15"/CN OR "AZIDE, MONOHYDRATE"/CN OR AZIDE-1-15N/CN OR AZIDE-15N2/CN OR AZIDE-15N3/CN OR AZIDE-2-15N/CN OR AZIDIAMANTANE/CN OR "AZIDIC ACID"/CN OR AZIDIN/CN OR AZIDIN-NAGANIN/CN OR AZIDINE/CN OR "AZIDINE FAST SCARLET 4BS"/CN OR "AZIDINE FAST SCARLET 7BS"/CN OR "AZIDINE FAST SCARLET GGS"/CN OR "AZIDINE YELLOW 5G"/CN OR AZIDIOL/CN OR AZIDITHION/CN OR AZIDO/CN OR "AZIDO RADICAL"/CN)
L16	16	SEA FILE=REGISTRY ABB=ON PLU=ON "AZIDE" AND L15
L18	545	SEA FILE=REGISTRY ABB=ON PLU=ON "AZID"
L19	3867	SEA FILE=HCAPLUS ABB=ON PLU=ON L16
L20	36392	SEA FILE=HCAPLUS ABB=ON PLU=ON L18
L21	141428	SEA FILE=HCAPLUS ABB=ON PLU=ON (N3 OR ?AZID? OR NITRENE OR SINGLET OXYGEN)
L22	2611	SEA FILE=HCAPLUS ABB=ON PLU=ON DYE(L) (L19 OR L20 OR L21)
L23	191092	SEA FILE=HCAPLUS ABB=ON PLU=ON ?CYANIN? OR ?RHODAMIN? OR ?PHENOXAZIN? OR ?PHENOTHIZIN? OR ?PHENOSELENAZIN? OR ?FLUORESCENCE IN? OR ?PORPHYRIN? OR ?BENZOPORPHYRIN? OR ?SQUARAIN? OR ?CORRIN? OR ?COROCONIUM? OR AZO(W)DYE OR METHIN?(W)DYE OR INDOLENIUM(W)DYE
L24	586	SEA FILE=HCAPLUS ABB=ON PLU=ON L22(L)L23
L27	13956	SEA FILE=HCAPLUS ABB=ON PLU=ON RECEPTOR(5A) (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)
L29	163257	SEA FILE=HCAPLUS ABB=ON PLU=ON (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)
L30	1	SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L24
L31	90	SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L23
L32	1	SEA FILE=HCAPLUS ABB=ON PLU=ON L21 AND L31
L33	2	SEA FILE=HCAPLUS ABB=ON PLU=ON L30 OR L32
L34	88	SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L21
L35	1	SEA FILE=HCAPLUS ABB=ON PLU=ON L34 AND L23
L38	4	SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L29
L39	53	SEA FILE=HCAPLUS ABB=ON PLU=ON L27(L)L23
L40	55	SEA FILE=HCAPLUS ABB=ON PLU=ON (L19 OR L20 OR L21) (L)L27
L44	318	SEA FILE=HCAPLUS ABB=ON PLU=ON HYPOCRELLIN?
L45	5	SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L44
L46	65735	SEA FILE=HCAPLUS ABB=ON PLU=ON HYPOCRELLIN? OR AZO OR METHINE OR INDOLENIUM
L47	429	SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L46
L48	429	SEA FILE=HCAPLUS ABB=ON PLU=ON L47 AND DYE
L50	1	SEA FILE=HCAPLUS ABB=ON PLU=ON L48 AND L29
L57	9	SEA FILE=HCAPLUS ABB=ON PLU=ON L39 AND PATENT/DT
L58	9	SEA FILE=HCAPLUS ABB=ON PLU=ON L57 AND PRD<20010307
L59	44	SEA FILE=HCAPLUS ABB=ON PLU=ON L39 NOT L57
L60	43	SEA FILE=HCAPLUS ABB=ON PLU=ON L59 AND PD<20010307
L61	52	SEA FILE=HCAPLUS ABB=ON PLU=ON L58 OR L60
L62	3	SEA FILE=HCAPLUS ABB=ON PLU=ON L40(L)CONJUGAT?
L63	3	SEA FILE=HCAPLUS ABB=ON PLU=ON L40 AND CONJUGAT?
L64	24	SEA FILE=HCAPLUS ABB=ON PLU=ON L40 AND (COVALENT? OR BOND? OR LINK?)

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L65 27 SEA FILE=HCAPLUS ABB=ON PLU=ON (L62 OR L63 OR L64)  
L66 3966 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 AND (L23 OR L46)  
L67 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L66 AND L29  
L68 26 SEA FILE=HCAPLUS ABB=ON PLU=ON L67 NOT (L65 OR L61 OR L50 OR  
L45 OR (L32 OR L33) OR L38 OR L35)  
L69 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L68 AND (CONJUGAT? OR  
RECEPTOR)

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L69 ANSWER 1 OF 7 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:284222 HCAPLUS  
 DOCUMENT NUMBER: 134:307611  
 TITLE: **Conjugated** polymer tag complexes and their preparation and use in assays  
 INVENTOR(S): Leif, Robert C.; Franson, Richard C.; Vallarino, Lidia  
 PATENT ASSIGNEE(S): USA  
 SOURCE: PCT Int. Appl., 104 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027625	A1	20010419	WO 2000-US27787	20001007
W: CA, CH, DE, FI, GB, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1999-158718P P 19991008  
 AB Processes are described for: (1) the sequential solid phase synthesis of polymers with at least one tag, which can be a light emitting and/or absorbing mol. species (optical-label), a paramagnetic or radioactive label, or a tag that permits the phys. sepn. of particles including cells. When multiple optical-labels are suitably arranged in three-dimensional space, the energy transfer from one mol. species to another can be maximized and the radiationless loss between members of the same mol. species can be minimized; (2) the coupling of these polymers to biol. active and/or biol. compatible mols. through peripheral pendant substituents having at least one reactive site; and (3) the specific cleavage of the coupled polymer from a solid phase support. The tagged-peptide or polymers produced by these processes and their **conjugates** with an analyte-binding species, such as a monoclonal antibody or a polynucleotide probe are described. When functionalized europium macrocyclic complexes, as taught in our U.S. patents 5,373,093 and 5,696,240, are bound to polylysine and other peptides, the emitted light increases linearly with the amt. of bound macrocyclic complex. Similar linearity will also result for multiple luminescent macrocyclic complexes of other lanthanide ions, such as samarium, terbium, and dysprosium, when they are bound to a polymer or mol.  
 REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:493550 HCAPLUS  
 DOCUMENT NUMBER: 133:101736  
 TITLE: A reagent system and method for increasing the luminescence of lanthanide(iii) macrocyclic complexes  
 INVENTOR(S): Leif, Robert C.; Vallarino, Lidia  
 PATENT ASSIGNEE(S): USA  
 SOURCE: PCT Int. Appl., 96 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042048	A1	20000720	WO 2000-US1211	20000118
W: CA, CH, DE, FI, GB, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1150985	A1	20011107	EP 2000-905653	20000118
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6340744	B1	20020122	US 2000-484670	20000118
PRIORITY APPLN. INFO.:				
			US 1999-116316P	P 19990119
			WO 2000-US1211	W 20000118

OTHER SOURCE(S): MARPAT 133:101736

AB Disclosed are a spectrofluorimetrically detectable luminescent compn. and processes for enhancing the luminescence of one or more lanthanide-contg. macrocycles. The luminescent compn. comprises a micelle-producing amt. of at least one surfactant, at least one energy transfer acceptor lanthanide element macrocycle compd. having an emission spectrum peak in the range from 500 to 950 nm, and a luminescence-enhancing amt. of at least one energy transfer donor compd. of yttrium or a 3-valent lanthanide element having at. no. 59-71, provided that the lanthanide element of said macrocycle compd. and the lanthanide element of said energy transfer donor compd. are not identical. The addn. of gadolinium(III) in the presence of other solutes to both the prototype and the difunctionalized europium, samarium, and terbium macrocyclic complexes, which were taught in our U.S. patents #5,373,093 and #5,696,240, enhances their luminescence. Similar enhancements of luminescence also results for the mono-functionalized europium, samarium, and terbium macrocyclic complexes, which were taught in our U.S. patent #5,696,240. The enhanced luminescence afforded by the compn. enables the detection and/or quantitation of many analytes in low concns. without the use of expensive, complicated time-gated detection systems.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:766507 HCAPLUS

DOCUMENT NUMBER: 130:29221

TITLE: Preparation of solid porous matrixes for pharmaceutical uses

INVENTOR(S): Unger, Evan C.

PATENT ASSIGNEE(S): Imarx Pharmaceutical Corp., USA

SOURCE: PCT Int. Appl., 139 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851282	A1	19981119	WO 1998-US9570	19980512
W: AU, BR, CA, CN, JP, KR, NZ				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 2002039594	A1	20020404	US 1998-75477	19980511
AU 9873787	A1	19981208	AU 1998-73787	19980512
EP 983060	A1	20000308	EP 1998-921109	19980512
R: DE, FR, GB, IT, NL				
US 2001018072	A1	20010830	US 2001-828762	20010409



## PRIORITY APPLN. INFO.:

US 1997-46379P P 19970513  
 US 1998-75477 A 19980511  
 WO 1998-US9570 W 19980512

AB A solid porous matrix formed from a surfactant, a solvent, and a bioactive agent is described. Thus, amphotericin nanoparticles were prep'd. by using ZrO<sub>2</sub> beads and a surfactant. The mixt. was milled for 24 h.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L69 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:466900 HCAPLUS

DOCUMENT NUMBER: 125:143229

TITLE: Preparation of novel nucleosides and oligomers.

INVENTOR(S): Cook, Phillip Dan; Teng, Kelly

PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 77 pp.

CODEN: PIXXD2

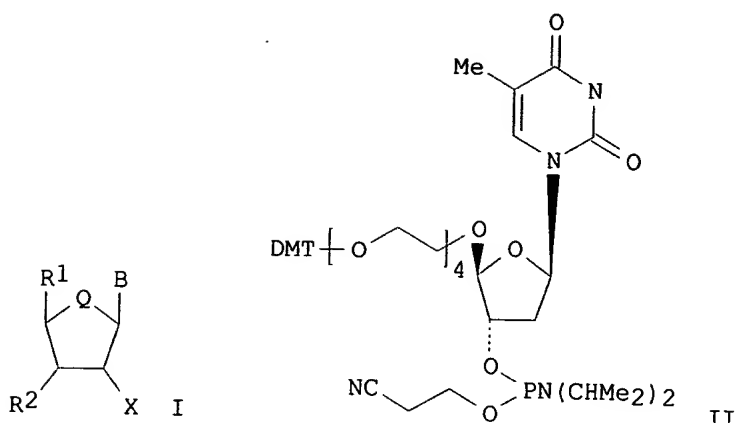
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 92

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610030	A1	19960404	WO 1995-US13038	19950929
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5608046	A	19970304	US 1994-314877	19940929
AU 9538923	A1	19960419	AU 1995-38923	19950929
US 5998603	A	19991207	US 1997-809239	19970520
AU 713740	B2	19991209	AU 1997-26244	19970624
AU 9726244	A1	19971106		
US 6232463	B1	20010515	US 1998-128508	19980804
PRIORITY APPLN. INFO.:			US 1994-314877	A2 19940929
			US 1990-558663	A2 19900727
			US 1990-566836	A2 19900813
			US 1991-703619	A2 19910521
			WO 1991-US5713	A 19910812
			WO 1992-US4294	A2 19920521
			US 1992-903160	B2 19920624
			AU 1993-38025	A3 19930225
			US 1993-39846	B2 19930330
			US 1994-150079	A3 19940407
			WO 1995-US13038	W 19950929
			US 1996-763354	A2 19961211
			US 1997-948151	A1 19971009
OTHER SOURCE(S):		MARPAT 125:143229		
GI				



AB Title compds. [I; B = nucleobase; X = H, OH, alkoxy, alkoxyalkyl, aminoalkoxy, F; R1 = N3, R3YeZ; Z = O, S, NH; Y = linker; e = 0, 1; R3 = alkyl, alkenyl, alkynyl, aryl, aralkyl, alkylaryl, phosphinyl, polyglycol, polyamine, polyether, (arom.) ring, **steroid**, reporter mol., peptide, protein, carbohydrate, reporter enzyme, terpene, phospholipid, intercalator, cell **receptor** binding mol., **porphyrin**, etc.; R2 = H, OH, activated phosphorus group, nucleoside, (activated) nucleotide, oligonucleotide, oligonucleoside, or protected deriv. thereof], and related compds., were prepd. Thus, phosphoramidite (II) was prepd. and used in solid phase synthesis of 5'-T\*GCATCCCCCAGGCCACCAT-3' (T\* = II-derived residue); the latter at 0.1  $\mu$ M gave 90.08% and 3.77% inhibition of VCAM-1 and ICAM-1 expression, resp., in bEND.3 murine endothelioma cells.

L69 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:739072 HCAPLUS

DOCUMENT NUMBER: 123:221117

TITLE: Identification of the bile acid binding proteins in human serum by photoaffinity labeling

AUTHOR(S): Kramer, Werner

CORPORATE SOURCE: SBU Metabolism, Hoechst Aktiengesellschaft, Frankfurt am Main, D-65926, Germany

SOURCE: Biochim. Biophys. Acta (1995), 1257(3), 230-8

CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The binding of **conjugated** and unconjugated bile acids to human serum lipoproteins was investigated by d. gradient centrifugation and photoaffinity labeling studies. The binding of bile acids to high-d. lipoprotein increased by substitution of the 3.alpha.-hydroxy group in cholate and taurocholate by a photolabile 3-**azido** or 3-**azi**-function. The affinity of bile acid derivs. to HDL showed the following ranking: 3.beta.-**azido**-7.alpha.,12.alpha.-dihydroxy-, 3,3-**azo**-7.alpha.,12.alpha.-dihydroxy- > 3.alpha.,7.alpha.,12.alpha.-trihydroxy-, 11.xi.-**azido**-3.alpha.,7.alpha.,12.xi.-trihydroxy- > 11.xi.-**azido**-12-oxo-3.alpha.,7.alpha.-dihydroxy- > 7,7-**azo**-3.alpha.,12.alpha.-dihydroxy-, 3.alpha.,7.alpha.-dihydroxy-, 3.alpha.,12.alpha.-dihydroxy- > 3.alpha.-hydroxy-cholan-24-oic acid. Based on the actual serum concns. of albumin and HDL, a preference of hydrophilic bile acids to HDL is evident, the 3-**azido**- and

3-azi-derivs. showing a 5-23-fold higher binding to HDL compared to sol. serum proteins. For the identification of the bile acid binding proteins in human blood, photoaffinity labeling with a variety of photolabile **conjugated** and unconjugated bile acid derivs. was performed with subsequent anal. of radiolabeled serum proteins by one- and two-dimensional gel electrophoresis. In addn. to albumin and the apolipoproteins A-I and A-II of high-d. lipoproteins (Kramer et al. (1979) Eur. J. Biochem. 102, 1-9), three further proteins in the lipoprotein free serum fraction of Mr 41,000, 50,000 and 83,000 were specifically labeled. By two-dimensional electrophoresis and by immunopptn. these proteins were identified as .alpha.1-acid glycoprotein (Mr 41,000), .alpha.1-antitrypsin (Mr 50,000) and transferrin (Mr 83,000). No binding of bile acids to haptoglobin, .alpha.2-HS-glycoprotein, hemopexin or .alpha.1-fetoprotein occurred. In conclusion, these studies show that bile acid derivs. bind to several serum proteins in addn. to albumin and furthermore that the substituent in position 3 of the **steroid** nucleus greatly influences the affinity of bile acids to high d. lipoproteins.

L69 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1994:271073 HCAPLUS  
 DOCUMENT NUMBER: 120:271073  
 TITLE: Derivatized oligonucleotides having improved uptake and other properties  
 INVENTOR(S): Manoharan, Muthiah; Cook, Philip Dan; Bennett, Clarence Frank  
 PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 73 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 92  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9307883	A1	19930429	WO 1992-US9196	19921023
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9229162	A1	19930521	AU 1992-29162	19921023
JP 06510791	T2	19941201	JP 1992-507961	19921023
EP 724447	A1	19960807	EP 1992-923139	19921023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
CA 2122030	C	19970304	CA 1992-2122030	19921023
US 6153737	A	20001128	US 1994-211882	19940422
AU 713740	B2	19991209	AU 1997-26244	19970624
AU 9726244	A1	19971106		
US 6114513	A	20000905	US 1997-924326	19970905
US 6232463	B1	20010515	US 1998-128508	19980804
US 6265558	B1	20010724	US 1999-383856	19990826
PRIORITY APPLN. INFO.:			US 1991-782374	A2 19911024
			US 1990-463358	B2 19900111
			US 1990-566977	B2 19900813
			WO 1991-US243	A2 19910111
			WO 1992-US9196	A 19921023
			AU 1993-38025	A3 19930225
			US 1993-116801	A2 19930903
			US 1994-211882	A2 19940422
			US 1995-458396	A1 19950602

US 1997-924326 A1 19970905

US 1997-948151 A1 19971009

AB Oligonucleotides were prepd. in which at least one of the nucleosides is functionalized at its 2'-position with a **steroid**, reporter, nonarom. lipophilic, enzyme, peptide, protein, vitamin, RNA cleaving complex, metal chelator, **porphyrin**, alkylating, hybrid photonuclease intercalator, or aryl **azide** photocrosslinking group. Thus, the phosphorothioate 5'-CHA-CsTsGsTsCsTsCsCsAsTsCsTsTsCsAsCsT (CHA = cholic acid) was prepd. and its cellular uptake measured by detg. the degree of acetylation of chloramphenicol by I-38 cells.

L69 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:599483 HCAPLUS

DOCUMENT NUMBER: 119:199483

TITLE: Glycosylated **steroid** derivatives for transport across biological membranes and process for making them

INVENTOR(S): Kahne, Daniel Evan; Walker Kahne, Suzanne

PATENT ASSIGNEE(S): Princeton University, USA

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

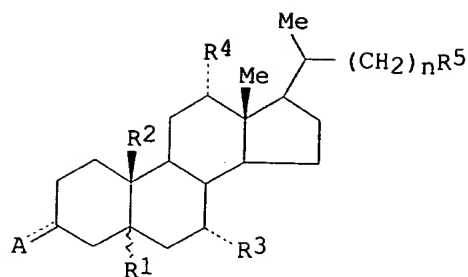
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9311772	A1	19930624	WO 1992-US10778	19921214
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KR, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SE, UA				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 5338837	A	19940816	US 1991-806985	19911213
AU 9332785	A1	19930719	AU 1993-32785	19921214
AU 665799	B2	19960118		
EP 618800	A1	19941012	EP 1993-901344	19921214
EP 618800	B1	19980527		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07503708	T2	19950420	JP 1992-511116	19921214
HU 70743	A2	19951030	HU 1994-1745	19921214
BR 9206927	A	19951121	BR 1992-6927	19921214
PL 171131	B1	19970328	PL 1992-304180	19921214
AT 166577	E	19980615	AT 1993-901344	19921214
ES 2118932	T3	19981001	ES 1993-901344	19921214
IL 104089	A1	19990509	IL 1992-104089	19921214
US 5455335	A	19951003	US 1994-224862	19940408
NO 9402165	A	19940801	NO 1994-2165	19940610
PRIORITY APPLN. INFO.:			US 1991-806985	19911213
			WO 1992-US10778	19921214
OTHER SOURCE(S):	MARPAT 119:199483			
GI				



AB Glycosylated **steroids I** [A = :O, OH, OR6, NR7R8, N3, NHCOR7, O2CAr, O2COR9, O2CR9, NCH2Ph; Ar = (substituted) Ph; a = single or double bond; R1 = H cis or trans to R2; R2 = Me; R3, R4 = H, OH, OR6; R5 = CO2R10, CH2OR9, CONH2, CONHR7, etc.; R6 = (protected) mono- or oligosaccharide; R7, R8 = H, alkyl, cycloalkyl, Ph, (CH2)f; f = 3-6; R9 = H, C1-3 alkyl; R10 = H, alkyl, alkenyl, alkynyl, Ph, CH2Ph] are provided which facilitate transport of therapeutic agents across biol. membranes and the blood-brain barrier. Thus, 3.alpha.-O-p-methoxybenzoyl-cis-5,10-bis-.alpha.,.alpha.-7,12-glucosylcholic acid Me ester enhanced the efficacy of the fungicides 10-thiastearic acid and 24-thiacholestanol against *Crithidia fasciculata*. 3.alpha.-O-benzoyl-cis-5,10-bis-.beta.,.beta.-7,12-glucosylcholic acid Me ester was prepd. by condensation of 2,3,4,6-tetra-O-(p-methoxy)benzylglucose sulfoxide with O3-benzoylcholic acid Me ester in the presence of 2,6-di-tert-butyl-4-methylpyridine, followed by reaction with triflic anhydride at -78.degree. and catalytic hydrogenation.

#2 of your request

CEPERLEY 09/898,885

=> d que 161

L23	191092	SEA FILE=HCAPLUS ABB=ON PLU=ON ?CYANIN? OR ?RHODAMIN? OR ?PHENOXAZIN? OR ?PHENOTHIZIN? OR ?PHENOSELENAZIN? OR ?FLUORESCEN? OR ?PORPHYRIN? OR ?BENZOPORPHYRIN? OR ?SQUARAIN? OR ?CORRIN? OR ?COROCONIUM? OR AZO(W)DYE OR METHIN?(W)DYE OR INDOLENIUM(W)DYE
L27	13956	SEA FILE=HCAPLUS ABB=ON PLU=ON RECEPTOR(5A) (SOMATOSTATIN OR BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)
L39	53	SEA FILE=HCAPLUS ABB=ON PLU=ON L27(L)L23
L57	9	SEA FILE=HCAPLUS ABB=ON PLU=ON L39 AND PATENT/DT
L58	9	SEA FILE=HCAPLUS ABB=ON PLU=ON L57 AND PRD<20010307
L59	44	SEA FILE=HCAPLUS ABB=ON PLU=ON L39 NOT L57
L60	43	SEA FILE=HCAPLUS ABB=ON PLU=ON L59 AND PD<20010307
L61	52	SEA FILE=HCAPLUS ABB=ON PLU=ON L58 OR L60

getting rid  
of patents &  
literature  
after the  
prior date

L61 combines the dyes of claim 1  
w/ the receptors of claim 2

=&gt; d ibib abs hitstr 1-10

L61 ANSWER 1 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:893678 HCAPLUS  
 TITLE: Recent progress in enantiomeric recognition of amino acid and its derivatives  
 AUTHOR(S): Mu, Qiming; Xue, Cuihua; Chen, Shuhua  
 CORPORATE SOURCE: Faculty of Chemistry, Sichuan University, Chengdu, 610064, Peop. Rep. China  
 SOURCE: Huaxue Yanjiu Yu Yingyong (2001), 13(5), 473-478  
 CODEN: HYYIFM; ISSN: 1004-1656  
 PUBLISHER: Huaxue Yanjiu Yu Yingyong Bianjibu  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: Chinese

AB A review with 60 refs. on recent progress in enantiomeric recognition of amino acid and its derivs. with subdivision headings: (1) chiral recognition of amino acid and its derivs. with **porphyrin** receptors; (2) chiral recognition of amino acid and its derivs. with cyclophane receptors; (3) chiral recognition of amino acid and its derivs. with cyclodextrin receptors; (4) chiral recognition of amino acid and its derivs. with crown ether receptors; (5) chiral recognition of amino acid and its derivs. with other macrocycles and polycyclic compds.; (6) chiral recognition of amino acid and its derivs. with guanidine salt mol. tweezers; (7) chiral recognition of amino acid and its derivs. with **steroid receptors**; and (8) conclusion.

L61 ANSWER 2 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:606352 HCAPLUS  
 DOCUMENT NUMBER: 135:313785  
 TITLE: Detection of progesterone receptors in human spermatozoa and their correlation with morphological and functional properties  
 AUTHOR(S): Contreras, H. R.; Llanos, M. N.  
 CORPORATE SOURCE: Unit of Reproduction, Physiology and Biophysic Programme, ICBM, Faculty of Medicine, University of Chile, Santiago, Chile  
 SOURCE: International Journal of Andrology (2001), 24(4), 246-252  
 CODEN: IJANDP; ISSN: 0105-6263  
 PUBLISHER: Blackwell Science Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB In previous reports, it has been demonstrated that progesterone (P) stimulates capacitation, hyperactivation of human sperm motility and initiates the acrosome reaction (AR). This last effect has been related to the presence of non-genomic **receptors** for the **steroid**, localized on the sperm head plasma membrane. These receptors can be detected after treating spermatozoa with the non-permeable conjugate progesterone-3-(O-carboxymethyl)oxime:bovine serum albumin-**fluorescein** isothiocyanate (P-BSA-FITC). In the present study, the presence of progesterone receptors was detd. in a selected sperm population with normal morphol. and high progressive motility. In addn., other parameters such as the AR, hypoosmotic swelling (HOS) test, stability of chromatin and capacitating effect of P were evaluated. The percentage of P-BSA-FITC pos.-spermatozoa present in the selected sperm population was higher than in total seminal spermatozoa. Furthermore, spermatozoa incubated with P showed a higher percentage motility and AR than did control spermatozoa. The HOS test indicated that membrane integrity of P-treated spermatozoa was not different to that found in the

control sperm suspensions. Unexpectedly, the total sperm population treated with P showed a marked susceptibility to nuclear decondensation with reducing agents. According to these results, the selected sperm population of this study, able to respond to P, may be similar to that with good motility and normal morphol. selected in the female reproductive tract, before fertilization.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 3 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:417261 HCAPLUS

DOCUMENT NUMBER: 135:16357

TITLE: Steroid compounds for steroid receptor binding assays

INVENTOR(S): Schoonen, Wilhelmus G. E. J.

PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.

SOURCE: PCT Int. Appl., 30 pp.

CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001040805	A1	20010607	WO 2000-EP11803	20001124 <--
W: US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				

PRIORITY APPLN. INFO.: EP 1999-204036 A 19991130 <--

OTHER SOURCE(S): MARPAT 135:16357

AB The invention provides a compd. having binding affinity for a **receptor** and comprising a **steroid** skeleton in its mol. structure, which compd. is Bu-A-Y-X-Ste (Bu = sterically bulky structure or mol. moiety having high affinity for a sterically bulky mol. structure; A = -NH-, -O-, -C(O)-, -S-; Y = branched or unbranched, satd. or unsatd. chain of 2 to 18 atoms of carbon, which chain is optionally interrupted by replacements of carbon atoms by oxygen, nitrogen or sulfur atoms and is optionally substituted with keto, hydroxyl, sulfhydryl or halogen groups; X = C or arylene group linked to the steroid skeleton with a carbon or an oxygen atom; Ste = group with a steroidal skeleton, having binding affinity for a **steroid receptor**; the bond between A and Y is optional double or triple bond; that between Y and X is optional double bond). The invention also provides for a method for detn. of binding between a compd. having a mol. group L in its mol. structure and a compd. having a mol. group R in its mol. structure, in which method L is the group Ste as defined above and R is a **steroid receptor**. An estradiol estrogen **receptor** ligand labeled with **allophycocyanin** (**steroid**-APC) was prepd. and assayed for binding with the .alpha.-estrogen receptor by time-resolved fluorescence resonance energy transfer assay.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 4 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:38760 HCAPLUS

DOCUMENT NUMBER: 134:202772

TITLE: Synthesis, characterization, and biological properties of **cyanine**-labeled **somatostatin** analogues as **receptor**-targeted fluorescent probes



AUTHOR(S): Licha, Kai; Hessenius, Carsten; Becker, Andreas;  
Henklein, Peter; Bauer, Michael; Wisniewski, Stefan;  
Wiedenmann, Bertram; Semmler, Wolfhard  
CORPORATE SOURCE: Institut fuer Diagnostikforschung GmbH an der Freien  
Universitaet Berlin, Berlin, 14050, Germany  
SOURCE: Bioconjugate Chemistry (2001), 12(1), 44-50  
CODEN: BCCHEs; ISSN: 1043-1802  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB We present the synthesis and characterization of the **somatostatin receptor**-specific peptide H2N-(D-Phe)-cyclo[Cys-Phe-(D-Trp)-Lys-Thr-Cys]-Thr-OH, which is labeled with a carboxylated indodicarbo- and an **indotricarbocyanine** dye at the N-terminal amino group. The prepn. was performed by automated solid-phase synthesis, with subsequent attachment of the **cyanine** dye and cleavage of the entire conjugate from the resin. The compds. display high molar absorbance and fluorescence quantum yields typical for **cyanine** dyes and are thus suitable receptor-targeted contrast agents for mol. optical imaging. The ability of these agents to target the **somatostatin receptor** was demonstrated by flow cytometry in vitro, in which the **indotricarbocyanine** conjugate led to elevated cell-assocd. fluorescence on **somatostatin receptor**-expressing tumor cells. In contrast, the corresponding linearized deriv. of the sequence H2N-(D-Phe)-Met-Phe-(D-Trp)-Lys-Thr-Met-Thr-OH produced only minimal cell fluorescence, hence confirming the specificity of the cyclic somatostatin analog. Intracellular localization could be visualized by near-IR (NIR) fluorescence microscopy. In conclusion, receptor-specific peptides are promising tools for designing site-directed optical contrast agents for use in mol. optical imaging.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 5 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:857684 HCAPLUS

DOCUMENT NUMBER: 135:170

TITLE: Lanreotide-induced modulation of 5-fluorouracil or mitomycin C cytotoxicity in human colon cancer cell lines: a preclinical study

AUTHOR(S): Tesei, A.; Ricotti, L.; De Paola, F.; Casini-Raggi, C.; Barzanti, F.; Frassinetti, G. L.; Zoli, W.

CORPORATE SOURCE: Istituto Oncologico Romagnolo, Forli, Italy

SOURCE: Journal of Chemotherapy (Firenze) (2000), 12(5), 421-430

CODEN: JCHEEU; ISSN: 1120-009X

PUBLISHER: E.I.F.T. srl

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The growth-inhibiting effect of the long-acting somatostatin analog lanreotide (LAN), alone or in combination with 5-fluorouracil (5-FU) and mitomycin C (MIT), was investigated in three human colon cancer lines. The inhibition of cell survival induced by LAN alone, as evaluated by the **sulforhodamine B** assay, ranged 20%-40% as a function of cell line and concn. An IC50 was never reached. The antiproliferative effect produced by a 48-h exposure to 5-FU or MIT was synergistically enhanced in all the cell lines by a subsequent 48-h exposure to LAN. This synergistic interaction was not related to specific cell cycle perturbations or to the expression of **somatostatin receptor 2** mRNA. LAN may be useful for enhancing the activity of 5-FU and MIT in colorectal cancer patients.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 6 OF 52 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:842014 HCAPLUS  
 DOCUMENT NUMBER: 134:21520  
 TITLE: Novel cyanine and indocyanine dye bioconjugates for biomedical applications  
 INVENTOR(S): Achilefu, Samuel; Dorshow, Richard Bradley; Bugaj, Joseph Edward; Rajagopalan, Raghavan  
 PATENT ASSIGNEE(S): Mallinckrodt Inc., USA  
 SOURCE: PCT Int. Appl., 38 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000071162	A2	20001130	WO 2000-US11060	20000426 <--
WO 2000071162	A3	20010705		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6217848	B1	20010417	US 1999-325769	19990604 <--
EP 1178830	A2	20020213	EP 2000-926343	20000426 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:				
			US 1999-135060P	P 19990520 <--
			US 1999-325769	A 19990604 <--
			WO 2000-US11060	W 20000426 <--

OTHER SOURCE(S): MARPAT 134:21520

AB Dye-peptide conjugates useful for diagnostic imaging and therapy are disclosed. The dye-peptide conjugates include several **cyanine** dyes with a variety of bis- and tetrakis(carboxylic acid) homologs. The small size of the compds. allows more favorable delivery to tumor cells as compared to larger mol. wt. imaging agents. The various dyes are useful over the range of 350-1300 nm, the exact range being dependent upon the particular dye. Use of dimethylsulfoxide helps to maintain the fluorescence of the compds. The mols. of the invention are useful for diagnostic imaging and therapy, in endoscopic applications for the detection of tumors and other abnormalities and for localized therapy, for photoacoustic tumor imaging, detection and therapy, and for sonofluorescence tumor imaging, detection and therapy. For example, monooctreotate-bisethylcarboxymethyl **indocyanine** dye (Cytate 1) was prepd. (yield of 80%) and evaluated in the CA20948 Lewis rat model of pancreatic acinar carcinoma. Using the CCD camera, strong localization of this dye was obsd. in the tumor at 90 min post injection. At 19 h post injection the animal was again imaged and tumor visualization was easily obsd. showing specificity of this agent for **somatostatin** receptors present in this tumor line.

L61 ANSWER 7 OF 52 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:516171 HCAPLUS  
 DOCUMENT NUMBER: 134:127990  
 TITLE: Novel receptor-targeted contrast agents for optical imaging of tumors  
 AUTHOR(S): Becker, Andreas; Hessenius, Carsten; Bhargava, Sarah; Ebert, Bernd; Sukowski, Uwe; Rinneberg, Herbert H.;

CORPORATE SOURCE: Wiedenmann, Bertram; Semmler, Wolfhard; Licha, Kai  
 Institut fuer Diagnostikforschung, Freie Univ. Berlin,  
 Berlin, Germany

SOURCE: Proceedings of SPIE-The International Society for  
 Optical Engineering (2000), 3924(Molecular  
 Imaging: Reporters, Dyes, Markers, and  
 Instrumentation), 41-47  
 CODEN: PSISDG; ISSN: 0277-786X

PUBLISHER: SPIE-The International Society for Optical Engineering

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Many gastroenteropancreatic tumors express **receptors** for **somatostatin** (SST) and/or vasoactive intestinal peptide (VIP). These receptors can be used as mol. targets for the delivery of contrast agents for tumor diagnostics. We have synthesized conjugates consisting of a **cyanine** dye and an SST analog or VIP for use as contrast agents in optical imaging. Receptor binding and internalization of these compds. were examd. with optical methods in transfected RIN38 tumor cells expressing the SST2 receptor or a GFP- labeled VIP (VPAC1) receptor. Furthermore, biodistribution of the conjugates was examd. by laser-induced fluorescence imaging in nude mice bearing SST2 or VPAC1 receptor-expressing tumors. After incubation of RIN38 SSTR2 cells in the presence of 100 nM **indotricarbocyanine**-SST analog, cell-assocd. fluorescence increased, whereas no increase was obsd. when receptor-mediated endocytosis was inhibited. **Indodicarbocyanine** -VIP accumulated in RIN38 VPAC1 cells and co-localization with the GFP-labeled VPAC1 receptor was obsd. After injection of **indotricarbocyanine**-SST analog into tumor-bearing nude mice, SST2 receptor-pos. tumors could be visualized for a time period from 10 min to at least 48 h. After application of **indodicarbocyanine**-VIP, a fluorescence signal in VIP1 receptor-expressing tumors was only detected during the first hour. We conclude that **cyanine** dye-labeled VIP and SST analog are novel, targeted contrast agents for the optical imaging of tumors expressing the relevant receptor.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 8 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:370600 HCAPLUS

DOCUMENT NUMBER: 133:249048

TITLE: Noninvasive monitoring of gene transfer using a reporter receptor imaged with a high-affinity peptide radiolabeled with 99mTc or 188Re

AUTHOR(S): Zinn, Kurt R.; Buchsbaum, Donald J.; Chaudhuri, Tandra R.; Mountz, James M.; Grizzle, William E.; Rogers, Buck E.

CORPORATE SOURCE: Departments of Radiology, Radiation Oncology, and Pathology, University of Alabama at Birmingham, Birmingham, AL, USA

SOURCE: Journal of Nuclear Medicine (2000), 41(5), 887-895

CODEN: JNMEAQ; ISSN: 0161-5505

PUBLISHER: Society of Nuclear Medicine, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Gene therapy protocols require better modalities to monitor the location and level of transferred gene expression. One potential in vivo mechanism to assess gene expression would be to image the binding of a radiolabeled peptide to a reporter receptor that is expressed in targeted tissues. This concept was tested in a tumor model using a replication-incompetent

adenoviral vector encoding the human type 2 **somatostatin receptor** (Ad5-CMVhSSTr2). Expression of the hSSTr2 reporter was imaged using a radiolabeled, somatostatin-avid peptide (P829). Methods: Bilateral s.c. A427 tumor xenografts were established on the flanks of athymic nude mice. These human-origin, non-small cell lung tumors are normally neg. for hSSTr2 expression. One tumor was injected directly with Ad5-CMVhSSTr2, whereas the second tumor was injected directly with a control Ad5 vector. The mice were injected i.v. 48 h later with P829 peptide that was radiolabeled to high specific activity with <sup>99m</sup>Tc (half-life, 6 h) or <sup>188</sup>Re (half-life, 17 h). Tumors were frozen and evaluated for **somatostatin receptor** expression using **fluorescein-labeled somatostatin**. Results: The accumulation of radiolabeled P829 in hSSTr2-expressing tumors was easily visualized by .gamma. camera imaging 3 h after injection. Imaging region of interest analyses and biodistribution studies confirmed a 5- to 10-fold greater accumulation of both radiolabeled P829 peptides in the Ad5-CMVhSSTr2-injected tumors vs. control tumors injected with control Ad5 vectors. Ad5-CMVhSSTr2-injected tumors accumulated 2.5-3.8 percentage injected dose per g 3 h after injection. Only Ad5-CMVhSSTr2-injected tumors expressed **somatostatin receptors**, as detd. by immunohistochem. Conclusion: These studies show the feasibility of imaging a <sup>99m</sup>Tc-labeled peptide's binding to a reporter receptor after in vivo gene transfer to tumor cells. The <sup>188</sup>Re-labeled peptide worked equally well for this imaging approach and offers the addnl. advantage of energetic .beta. decay with potential therapeutic efficacy. <sup>99m</sup>Tc and <sup>188</sup>Re are generator produced, an advantage for widespread availability and low cost, and both radioisotopes can be imaged with existing, high-resoln. modalities. There is great potential for using <sup>99m</sup>Tc-labeled peptides for imaging gene transfer with the hSSTr2 reporter receptor, esp. when the reporter correlates with the expression of therapeutic genes that can be included simultaneously in the gene therapy vector.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 9 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:241336 HCAPLUS

DOCUMENT NUMBER: 133:70934

TITLE: Two-dimensional fluorescence intensity distribution analysis: theory and applications

AUTHOR(S): Kask, Peet; Palo, Kaupo; Fay, Nicolas; Brand, Leif; Mets, Ulo; Ullmann, Dirk; Jungmann, Joern; Pschorr, Johannes; Gall, Karsten

CORPORATE SOURCE: EVOTEC BioSystems AG, Hamburg, D-22525, Germany

SOURCE: Biophysical Journal (2000), 78(4), 1703-1713

CODEN: BIOJAU; ISSN: 0006-3495

PUBLISHER: Biophysical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A method of sample anal. is presented which is based on fitting a joint distribution of photon count nos. In expts., fluorescence from a microscopic vol. contg. a fluctuating no. of mols. is monitored by two detectors, using a confocal microscope. The two detectors may have different polarizational or spectral responses. Concns. of fluorescent species together with two specific brightness values per species are detd. The two-dimensional fluorescence intensity distribution anal. (2D-FIDA), if used with a polarization cube, is a tool that is able to distinguish fluorescent species with different specific polarization ratios. As an example of polarization studies by 2D-FIDA, binding of 5'-(6-carboxytetramethylrhodamine) (TAMRA)-labeled theophylline to an anti-theophylline antibody has been studied. Alternatively, if two-color

equipment is used, 2D-FIDA can det. concns. and specific brightness values of fluorescent species corresponding to individual labels alone and their complex. As an example of two-color 2D-FIDA, binding of TAMRA-labeled somatostatin-14 to the human type-2 high-affinity **somatostatin receptors** present in stained vesicles has been studied. The presented method is unusually accurate among fluorescence fluctuation methods. It is well suited for monitoring a variety of mol. interactions, including receptors and ligands or antibodies and antigens.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L61 ANSWER 10 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:806861 HCAPLUS

DOCUMENT NUMBER: 130:47464

TITLE: The utilization of fusion proteins composed of a receptor protein and a fluorescein protein in order to study drug targeting

INVENTOR(S): Galzi, Jean-luc; Alix, Philippe

PATENT ASSIGNEE(S): Centre National de la Recherche Scientifique, Fr.

SOURCE: PCT Int. Appl., 104 pp.

CODEN: PIXXD2

DOCUMENT TYPE: **Patent**

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9855873	A2	19981210	WO 1998-FR1136	19980604 <--
WO 9855873	A3	19990304		
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2764387	A1	19981211	FR 1997-6977	19970605
FR 2764387	B1	19990723		
EP 986759	A2	20000322	EP 1998-929488	19980604 <--
R: DE, FR, GB, IT				
JP 2002504998	T2	20020212	JP 1999-501738	19980604 <--
PRIORITY APPLN. INFO.: FR 1997-6977 A 19970605 <--				
WO 1998-FR1136 W 19980604 <--				

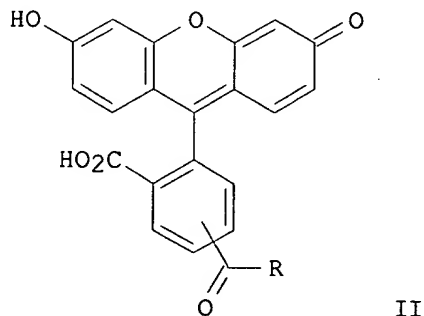
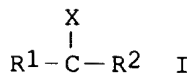
AB The invention concerns the construction and application of fusion proteins composed of a receptor protein, protein G and a fluorescent protein in order to study drug-receptor interactions by using labeled compds. that either excite the fusion protein or are excited by it as a result of binding. Fusion proteins should have a molar extinction coeff. of at least  $1.4 \times 10^4$  M<sup>-1</sup>cm<sup>-1</sup> and a quantum yield of at least 0.38. Fluorescent proteins of the fusion proteins are green fluorescent protein (GFP), enhanced green fluorescent protein (EGFP), yellow fluorescent protein (YFP) and enhanced yellow fluorescent protein (EYFP), their derivs., mutants, and fragments. Receptor proteins in the fusion proteins are membrane receptors coupled to protein G, growth factor **receptor**, insulin **receptors**, channel **receptors**, **steroid receptors** etc. Labels for the target mols. are either receptors or donors in the energy transfer during fluorescence; in the case of EGFP, the energy acceptors bodipy, eosine, erythrosine etc. can be used; energy donors for EGFP are e.g. violet acids, alizarines, etc. Host cells for gene expression are mammalian cells, yeast, fungi, virus infected insect cells. Thus a DNA fusion sequence was constructed contg. EGFP gene and the NK2R tachykinin receptor gene; the protein was expressed in HEK 293 cells. Neurokinin A was labeled with bodipy, eosine, and

**sulforhodamine 101** and the labeled compds. were used for targeting. Fluorescence of the cell culture was measured; than cells were incubated with one of the labeled neurokinin A compds.; the change in the fluorescent signal was recorded. Real time inhibition could be recorded by adding competing mols., e.g. SR 48968, or the cyclopeptide cyclo(-Gln-Trp-Phe-Gly-Leu-Met); and recording appearance of the original fluorescence spectrum.

=> d ibib abs hitstr 11-52

L61 ANSWER 11 OF 52 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:684447 HCAPLUS  
 DOCUMENT NUMBER: 129:290446  
 TITLE: Preparation of fluorescent somatostatin analogs for receptor binding studies  
 INVENTOR(S): Vincent, Jean-Pierre; Gaudriault, Georges; Beaudet, Alain  
 PATENT ASSIGNEE(S): Advanced Bioconcept, Inc., Can.  
 SOURCE: U.S., 13 pp. Cont.-in-part of U.S. 5,693,679.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5824772	A	19981020	US 1995-475751	19950607 <--
US 5693679	A	19971202	US 1995-416007	19950404
WO 9631531	A2	19961010	WO 1996-CA207	19960404 <--
WO 9631531	A3	19970220		
W: AT, CH, DE, DK, ES, GB, LU, PT, SE				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 820466	A2	19980128	EP 1996-908950	19960404 <--
R: BE, CH, DE, DK, FR, GB, IT, LI, NL, SE, IE, FI				
US 6054557	A	20000425	US 1996-682810	19960710 <--
PRIORITY APPLN. INFO.:			US 1995-416007	19950404 <--
			US 1995-475751	19950607 <--
			US 1995-504856	19950720 <--
			WO 1996-CA207	19960404 <--
OTHER SOURCE(S):		MARPAT 129:290446		
GI				



AB Light-emitting compds. I [R1 = light-emitting moiety; R2 = Y-Z-Q; Y, Q independently = chain of 1-40 amino acid residues; Z = Phe-Phe-Trp-Lys-Thr, Phe-Phe-D-Trp-Lys-Thr; X = O, S, OH, CO, NH, H, OR, NR, R, R6R3R4; each R, R6, R4, R3 independently = H, (un)branched, (un)substituted C1-6 alkyl] pharmaceutically acceptable salts or complexes thereof. The peptide is linked at a first amino acid position to (C-X), and the light-emitting compd. exhibits substantial biol. activity in the presence of a **receptor** having affinity for **somatostatin**-based peptides. Thus, coupling of **fluorescein** active ester II (R = N-succinimidyl) with [D-Trp8]-somatostatin(1-14) to give the corresponding fluorescent peptide II [R = Ala-Gly-Cys-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-Cys-OH cyclic disulfide] (III). Fluorescent labeled peptide III showed binding to **somatostatin receptors**, with IC50 = 3.2 nM vs. IC50 = 0.26 for the unlabeled peptide.

L61 ANSWER 12 OF 52 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:608078 HCAPLUS  
 DOCUMENT NUMBER: 129:298610  
 TITLE: Functional antagonism of gonadal steroids at the 5-hydroxytryptamine type 3 receptor  
 AUTHOR(S): Wetzel, Christian H. R.; Hermann, Bettina; Behl, Christian; Pestel, Elmar; Rammes, Gerhard; Zieglgansberger, Walter; Holsboer, Florian; Rupprecht, Rainer  
 CORPORATE SOURCE: Max Planck Institute of Psychiatry, Munich, 80804, Germany  
 SOURCE: Mol. Endocrinol. (1998), 12(9), 1441-1451  
 CODEN: MOENEN; ISSN: 0888-8809  
 PUBLISHER: Endocrine Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Steroid hormone action involves binding to cognate intracellular receptors that, in turn, bind to resp. response elements and thus modulate gene expression. The present study shows that the gonadal steroids, 17.β.-estradiol and progesterone, may also act as functional antagonists at the 5-hydroxytryptamine type 3 (5-HT3) receptor in whole-cell voltage-clamp recordings of HEK 293 cells stably expressing the 5-HT3 receptor. Functional antagonistic properties at this ligand-gated ion channel could also be shown for 17.α.-estradiol, 17.α.-ethinyl-17.β.-estradiol, mestranol, R 5020, testosterone, and allopregnanolone but not for pregnenolone sulfate and cholesterol. An antagonism at the 5-HT3 receptor could further be obsd. with the arom. alc. 4-dodecylphenol but not with phenol or ethanol. Thus, the modulation of 5-HT3 **receptor** function by **steroids** or alcs. is dependent on their resp. structure. The antagonistic action of **steroids** at the 5-HT3 **receptor** is not mediated via the serotonin binding site because the steroids did not alter the binding affinity of [3H]GR65630 to the 5-HT3 receptor, and kinetic expts. revealed a quite different response pattern to 17.β.-estradiol when compared with the competitive antagonist metoclopramide. BSA-conjugated gonadal steroids labeled with **fluorescein** isothiocyanate bound to membranes of HEK 293 cells expressing the 5-HT3 receptor in contrast to native HEK 293 cells. However, there was no dose-dependent displacement of the binding of gonadal steroids to membranes of cells expressing the 5-HT3 receptor in binding expts. or fluorescence studies. Thus, gonadal steroids probably interact allosterically with the 5-HT3 receptor at the receptor-membrane interface. The functional antagonism of gonadal **steroids** at the 5-HT3 **receptor** may play a role for the

development and course of nausea during pregnancy and of psychiatric disorders.

L61 ANSWER 13 OF 52 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:112498 HCAPLUS  
 DOCUMENT NUMBER: 128:176476  
 TITLE: A method for quantitating competitive binding of molecules to steroid hormone receptors utilizing fluorescence polarization  
 INVENTOR(S): Bolger, Randall E.; Ervin, Kerry M.; Lowery, Robert G.; Checovich, William J.  
 PATENT ASSIGNEE(S): Panvera Corp., USA; Burke, Thomas, J.  
 SOURCE: PCT Int. Appl., 37 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9805962	A1	19980212	WO 1997-US13538	19970801 <--
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
PRIORITY APPLN. INFO.: US 1996-23034P P 19960802 <--				
AB The system comprises mixing a fluorescence-emitting compd. that binds to the steroid hormone receptors, particularly the estrogen receptor, in a soln. contg. the steroid hormone receptors. Then, measuring the fluorescence polarization of the soln. Subsequently, incubating the soln. with at least one mol. that may compete with the compd. for interaction with the steroid hormone receptors. Measuring the fluorescence polarization of the soln. again. Finally, comparing the fluorescence polarization measurements to quantify any competitive interaction. A fluorescence-emitting compd. such as a fluorescence-emitting hormone can be used in combination with a fluorophore covalently coupled to an oligonucleotide to study how hormone and oligonucleotide binding to the hormone receptor are affected by each other.				

L61 ANSWER 14 OF 52 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:633567 HCAPLUS  
 DOCUMENT NUMBER: 127:303487  
 TITLE: Bombesin-like peptides stimulate somatostatin release from rat fundic D cells in primary culture  
 AUTHOR(S): Schaffer, Kirsten; Herrmuth, Hedda; Mueller, James; Coy, David H.; Wong, Helen C.; Walsh, John H.; Classen, Meinhard; Schusdziarra, Volker; Schepp, Wolfgang  
 CORPORATE SOURCE: Dep. Med. II and Pathology, Technical Univ., Munich, D-81675, Germany  
 SOURCE: Am. J. Physiol. (1997), 273(3, Pt. 1), G686-G695  
 CODEN: AJPHAP; ISSN: 0002-9513  
 PUBLISHER: American Physiological Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB In several species, bombesin-like neuropeptides stimulate somatostatin release in in vitro prepsns. of gastric mucosa. We sought to det. if this response is due to a direct effect on fundic D cells. Rat fundic mucosal cells were isolated by pronase E (1% D cells). D cells were sepd. by counterflow elutriation and subsequent d.-gradient centrifugation (Nycodenz) (15% D cells) and grown in primary culture for 48 h (46% D



cells). Cultured cells were double stained with affinity-purified rabbit-anti- gastrin-releasing peptide (GRP) receptor antibody and mouse monoclonal antibody to human somatostatin. After incubation with **rhodamine**-labeled anti-rabbit and **fluorescein** isothiocyanate-labeled anti-mouse antibodies, reactions were visualized by fluorescence microscopy. All cells pos. for **somatostatin** had GRP **receptors**, whereas all non-D cells showed no expression in this G cell-free culture system. Somatostatin release from cultured cells was stimulated by sulfated cholecystokinin octapeptide (CCK-8; EC50  $3 \times 10^{-10}$  M) and epinephrine (EC50  $4 \times 10^{-8}$  M), which are established stimuli for canine fundic D cells. Bombesin (EC50  $6 \times 10^{-11}$  M), its mammalian analog GRP-27, and neuromedin C (GRP-10) (EC50  $1 \times 10^{-10}$  M, for both) were almost equally potent stimuli of somatostatin release, eliciting maximal response at  $10^{-9}$  M (400-550% above basal). Neuromedin B was less potent and effective (maximal response at  $10^{-8}$  M, 230% above basal). [D-Phe6]bombesin-(6-13)-OMe, a specific **bombesin** receptor antagonist, inhibited **bombesin**-stimulated **somatostatin** release in a competitive manner (IC50  $9 \times 10^{-8}$  M). Potentiating interactions were obsd. between bombesin and dibutyryl adenosine 3',5'-cyclic monophosphate (dbcAMP) or epinephrine, but not between bombesin and CCK-8. We conclude that bombesin-like peptides directly stimulate **somatostatin** release by interacting with specific **receptors** on rat fundic D cells. Bombesin-like peptides appear to induce  $\text{Ca}^{2+}$ -phospholipid-dependent signal-response transduction, as is indirectly suggested by potentiating interactions with dbcAMP or epinephrine.

L61 ANSWER 15 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:86681 HCAPLUS

DOCUMENT NUMBER: 126:166609

TITLE: Membrane binding sites and non-genomic effects of estrogen in cultured human preosteoclastic cells

AUTHOR(S): Fiorelli, Gianna; Gori, Francesca; Frediani, Uliana; Franceschelli, Francesco; Tanini, Annalisa; Tosti-Guerra, Cristina; Benvenuti, Susanna; Gennari, Luigi; Becherini, Lucia; Brandi, Maria Luisa

CORPORATE SOURCE: Dep. Clinical Physiopathology; Univ. Florence, Florence, 50139, Italy

SOURCE: J. Steroid Biochem. Mol. Biol. (1996), 59(2), 233-240

CODEN: JSBBEZ; ISSN: 0960-0760

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Besides functional estrogen receptors, the presence of signaling cell surface binding sites for 17.β-estradiol (17.β.E2) has been reported in osteoblast- and osteoclast-like cells, suggesting that 17.β.E2 may influence bone remodelling by a dual mechanism of action: to affect gene expression mediated by the nuclear activity of the **steroid-receptor** complex, and to initiate rapid responses triggered by a signal-generating receptor on the cell surface. Recently, we demonstrated that the human preosteoclastic cell line FLG 29.1 bears functional estrogen receptors. In this study, we examd. FLG 29.1 cells for the presence of cell surface binding sites for 17.β.E2, and whether 17.β.E2 could elicit cell signaling. Using a cell-impermeant and fluorescent estrogen conjugate, 17.β-estradiol-6-carboxymethyl oxime-bovine serum albumin-**fluorescein** isothiocyanate, we demonstrated the presence of specific plasma membrane binding sites for 17.β.E2. Stimulation of FLG 29.1 cells with low (1 nM) and high (1 .μM) doses of 17.β.E2 induced a prompt and

significant increase of cellular pH, as measured in single cells using an image anal. system. In addn., both cAMP and cGMP were significantly increased by 17.beta.E2 with a dose-dependent response. Finally, a rapid increase of intracellular calcium ion concn. was also induced by 1 nM 17.beta.E2, as measured in single cells using an image anal. system. Our findings strongly suggest a non-genomic action of 17.beta.E2 on osteoclast precursors.

L61 ANSWER 16 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:3193 HCAPLUS

DOCUMENT NUMBER: 126:55101

TITLE: Differential internalization of somatostatin in COS-7 cells transfected with SST1 and SST2 receptor subtypes: a confocal microscopic study using novel fluorescent somatostatin derivatives

AUTHOR(S): Nouel, Dominique; Gaudriault, Georges; Houle, Mariette; Reisine, Terry; Vincent, Jean-Pierre; Mazella, Jean; Beaudet, Alain

CORPORATE SOURCE: Montreal neurological Institute, McGill University, Montreal, PQ, H3A 2B4, Can.

SOURCE: Endocrinology (1997), 138(1), 296-306

CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A growing body of evidence suggests that neuropeptide binding to G protein-linked receptors may result in internalization of receptor-ligand complexes, followed by intracellular mobilization and degrdn. of the ligand into its target cells. Because of discrepant results in the literature concerning the occurrence of such a mechanism for the tetradecapeptide somatostatin (SRIF), the authors have re-investigated this question by comparing the binding and internalization of iodinated and fluorescent derivs. of the metabolically stable analog of SRIF, [D-Trp8]SRIF, in COS-7 cells transfected with cDNA encoding the SST1 or SST2A receptor subtype. A series of fluoresceinyl and Bodily fluorescent derivs. of [D-Trp8]SRIF-14 was purified by HPLC, analyzed for purity by mass spectrometry, and tested for biol. activity in a membrane binding assay. Of the six compds. tested, fluoresceinyl and Bodily derivs. labeled in position .alpha. (fluo-SRIF) retained high affinity for SRIF receptors. COS-7 cells transfected with cDNA encoding either SST1 or SST2A receptors both displayed specific, high affinity binding of iodinated and fluo-SRIF. At 4 C, the labeling was confined to the cell surface in both cell types, as indicated by the fact that it was entirely removable by a hypertonic acid wash and assumed a pericellular distribution in the confocal microscope. At 37 C, the fate of specifically bound ligand varied markedly according to the type of receptor transfected. In cells encoding the SST1 receptor, approx. 20% of specifically bound ligand was recovered in the acid-resistant (i.e. intracellular) fraction. This fraction remained clustered at the periphery of the cell, suggesting That it was being sequestered either within or immediately beneath the plasma membrane. By contrast, in cells transfected with SST2A receptors, up to 75% of the specifically bound ligand was recovered inside the cells, where it clustered into small endosome-like particles. These particles increased in size and moved toward the nucleus with time, suggestive of receptor-ligand complexes proceeding down the endocytic pathway. These result demonstrate that neuropeptides may be processed differently depending on the subtype of receptor expressed in their target cells and suggest that these different processing patterns may reflect different modes of sensitization/desensitization and recycling of the receptors, and thereby

of transmembrane signaling.

L61 ANSWER 17 OF 52 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:603971 HCAPLUS  
 DOCUMENT NUMBER: 125:234201  
 TITLE: Part i. photophysics and excited state dynamics of  
**porphyrin** dimers and trimers, and, part ii.  
 modulation of GABA(a) **receptors** by  
**steroids** and **steroid** analogs in  
 cultured rat hippocampal neurons  
 AUTHOR(S): Wittmer, Lisa Lynn  
 CORPORATE SOURCE: Washington Univ., St. Louis, MO, USA  
 SOURCE: (1996) 181 pp. Avail.: From degree-granting  
 institution  
 From: Diss. Abstr. Int., B 1996, 57(5), 3224  
 DOCUMENT TYPE: Dissertation  
 LANGUAGE: English  
 AB Unavailable

L61 ANSWER 18 OF 52 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:622950 HCAPLUS  
 DOCUMENT NUMBER: 123:1401  
 TITLE: Somatodendritic internalization and perinuclear  
 targeting of neurotensin in the mammalian brain  
 AUTHOR(S): Faure, Marie-Pierre; Alonso, Angel; Nouel, Dominique;  
 Gaudriault, Georges; Dennis, Michael; Vincent,  
 Jean-Pierre; Beaudet, Alain  
 CORPORATE SOURCE: Montreal Neurol. Inst., Montreal, PQ, H3A 2B4, Can.  
 SOURCE: J. Neurosci. (1995), 15(6), 4140-7  
 CODEN: JNRSDS; ISSN: 0270-6474  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Polypeptide hormones and growth factors have long been known to  
 internalize into peripheral target cells as a result of their interaction  
 with cell surface receptors. Studies in culture have suggested that  
 certain neuropeptides might undergo a similar type of translocation in  
 neurons. To investigate this possibility in adult mammalian brain, we  
 have examd. by confocal laser microscopy the events that follow the  
 binding of **fluorescein**-tagged derivs. of the tridecapeptide  
 neurotensin to basal forebrain cholinergic cells. Our results demonstrate  
 a selective time- and temp.-dependent internalization of fluo-neurotensin  
 in these cells. This internalization is receptor mediated, proceeds from  
 the entire somatodendritic membrane of the cells, and utilizes  
 endosome-like organelles which are mobilized from dendrites to perikarya  
 and from the periphery of the cell to its perinuclear region. Parallel  
 studies carried out on Sf9 insect cells expressing the rat  
**neurotensin receptor** from a recombinant baculovirus  
 indicated that the internalization process involves receptor-ligand  
 complexes and not merely the fluorescent peptide itself. These data  
 suggest that receptor internalization plays a role in neuropeptide  
 signaling in the brain and that it can be harnessed for selective  
 identification of neuropeptide target cells.

L61 ANSWER 19 OF 52 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1995:219105 HCAPLUS  
 DOCUMENT NUMBER: 122:133002  
 TITLE: Preparation of antineoplastic agents having increased  
 activity.  
 INVENTOR(S): Eisenbrand, Gerhard; Roth, Thomas  
 PATENT ASSIGNEE(S): Germany

SOURCE: Ger. Offen., 9 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: **Patent**  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4309344	A1	19940929	DE 1993-4309344	19930323
WO 9421265	A1	19940929	WO 1994-EP901	19940322 <--

W: JP, US

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: DE 1993-4309344 19930323 <--

OTHER SOURCE(S): MARPAT 122:133002

AB The title compds. (R2)(R3)C(OR4)OCH2R1 [I; R1 = H, Me, Et; R2 = H, Me; R3 = (un)substituted cytotoxic substituent with affinity to **steroid receptors**, carrier with DNA affinity, (un)satd. alkyl; R4 = cytotoxic function, etc.], useful as antineoplastic agents, are prepd. Thus, acridine deriv. II was prepd. and demonstrated a IC50 in a **sulforhodamine B** assay using the MCF-7 cell line of 3.7 .mu.M (calcd. as 4-hydroperoxycyclophosphamide).

L61 ANSWER 20 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:693770 HCAPLUS

DOCUMENT NUMBER: 121:293770

TITLE: Neurotensin peptide analogs labeled with fluorescent dyes as probes for the detection of neurotensin receptors

INVENTOR(S): Faure, Marie-Pierre; Faure, Marie-pierre; Gaudreau, Pierrette

PATENT ASSIGNEE(S): McGill University, Can.

SOURCE: Eur. Pat. Appl., 19 pp.

CODEN: EPXXDW

DOCUMENT TYPE: **Patent**

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 606804	A2	19940720	EP 1993-403185	19931227 <--
EP 606804	A3	19950524		
EP 606804	B1	20011004		

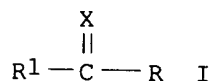
R: BE, CH, DE, FR, GB, LI, SE

CA 2086453 AA 19940701 CA 1992-2086453 19921230

PRIORITY APPLN. INFO.: CA 1992-2086453 A 19921230 <--

OTHER SOURCE(S): MARPAT 121:293770

GI



AB Compds. I or their pharmaceutically acceptable salts (R = -Y-Arg-Pro-Z-Ile-Leu, Y = Arg, Z = Tyr, Trp; R1 = **fluorescein**, **rhodamine**, Blue fluorescent and Texas red; X = O or S) are

described for use as labels for cell surface **neurotensin receptors**. These compds., derivs. of neurotensin, can be used in the isolation of cells presenting the receptor on the cell surface. The synthesis of [1-glutamic acid] neurotensin and its labeling with **fluorescein** are demonstrated. The use of the probes to detect the receptor in rat brain is demonstrated.

L61 ANSWER 21 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:676856 HCAPLUS

DOCUMENT NUMBER: 121:276856

TITLE: Epidermal cell fate determination in Arabidopsis: patterns defined by a steroid-induced regulator

AUTHOR(S): Lloyd, Alan M.; Schena, Mark; Walbot, Virginia; Davis, Ronald W.

CORPORATE SOURCE: Department Biochemistry, Stanford Univ., Stanford, CA, 94305, USA

SOURCE: Science (Washington, D. C.) (1994), 266(5184), 436-9

CODEN: SCIEAS; ISSN: 0036-8075

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The Arabidopsis mutant ttg lacks both trichomes (epidermal hairs) and **anthocyanin** pigments. Trichomes and **anthocyanins** are restored by the constitutive expression of the maize transcriptional regulator (R). The expression of an R-glucocorticoid **receptor** chimeric protein results in a **steroid** hormone-dependent, conditional allele of R that functions in whole Arabidopsis plants. The response of the chimeric protein to pulses of hormone was used to define the patterns and timing of trichome formation on the developing leaf epidermis. Each adaxial epidermal leaf cell appears to have an equal probability of differentiating into a trichome; there is a temporal zone of decision for trichome cell fate that proceeds as a wave from the tip to the base of developing leaves.

L61 ANSWER 22 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:646737 HCAPLUS

DOCUMENT NUMBER: 121:246737

TITLE: Neurotensin promotes oscillatory bursting behavior and is internalized in basal forebrain cholinergic neurons

AUTHOR(S): Alonso, Angel; Faure, Marie-Pierre; Beaudet, Alain

CORPORATE SOURCE: Montreal Neurological Inst., McGill Univ., Montreal, PQ, H3A-2B4, Can.

SOURCE: J. Neurosci. (1994), 14(10), 5778-92

CODEN: JNRSDS; ISSN: 0270-6474

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cholinergic neurons of the basal forebrain magnocellular complex (BF) constitute the primary source of acetylcholine to the cerebral cortex and are thought to be instrumental in mediating cortical activation and plasticity. Recent light and electron microscopic studies have revealed a selective assocn. of **receptors** for the neuropeptide **neurotensin** (NT) with BF cholinergic neurons, suggesting that this peptide may be playing a key role in the control of BF cholinergic function. In the present study, the authors have investigated by intracellular recording in guinea pig brain slices the neuromodulatory actions of NT on the intrinsic excitability of BF cholinergic neurons that were identified electrophysiol. by their low-threshold discharge, slow afterhyperpolarization, and transient outward rectification (TOR). In all cholinergic neurons tested, bath application of NT (20-200 nM for 1-4 min) produced, via a direct mechanism, a membrane potential depolarization

assocd. with a decrease in apparent input conductance. Most significantly, NT led to the emergence of a very prominent slow rhythmic bursting pattern that could shape into complex spindle-like sequences that were intrinsically generated by the cholinergic cells. These NT actions were also accompanied by a redn. of both the slow afterhyperpolarization and TOR. Bursting oscillations relied on the activation of  $\text{Ca}^{2+}$  conductances as opposed to  $\text{Na}^{+}$  conductances, since they were absent during  $\text{Ca}^{2+}$ -conductance block with  $\text{Mn}^{2+}$ , but still occurred in the presence of the  $\text{Na}^{+}$ -channel blocker TTX. NT actions were specific, since they could be reproduced by application of the active (NT 8-13) but not of the inactive (NT 1-8) fragment of the peptide. Identification of the BF cholinergic neurons as direct NT targets was further provided by confocal laser scanning microscopic demonstration of internalization of a **fluoresceinylated** deriv. of NT (fluo-NT) within biocytin-filled, electrophysiol. identified cholinergic neurons. The results demonstrate the electrophysiol. functionality of NT receptors on BF cholinergic neurons and the existence of a receptor-mediated internalization of NT in these cells. They also suggest that the peptide is an important player in the control of BF function and, in particular, in the generation of forebrain network oscillations.

L61 ANSWER 23 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:527652 HCAPLUS

DOCUMENT NUMBER: 121:127652

TITLE: The somatostatin analog octreotide protects against ethanol-induced microcirculatory stasis and elevated vascular permeability in rat gastric mucosa

AUTHOR(S): Kusterer, Klaus; Buchheit, Karl-Heinz; Schade, Anja; Bruns, Christian; Neuberger, Christoph; Engel, Guenter; Usadel, Klaus H.

CORPORATE SOURCE: Johann Wolfgang Goethe-University, Center of Internal Medicine, Department of Endocrinology, Theodor Stern Kai 7, Frankfurt am Main, 60590, Germany

SOURCE: Eur. J. Pharmacol. (1994), 259(3), 265-71  
CODEN: EJPHAZ; ISSN: 0014-2999

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors investigated the effect of two somatostatin derivs., octreotide and 5-(L)-citrullin-octreotide, on ethanol-induced hemorrhagic lesions, microcirculatory stasis and elevated vascular permeability in the rat stomach, with the goal to elucidate the pharmacol. and microcirculatory mechanisms behind the gastroprotective effect. Radioligand studies revealed a high affinity of octreotide for the **somatostatin receptor** ( $\text{IC}_{50} = 5 \cdot 10^{-10} \text{ mol/L}$ ), in contrast to 5-(L)-citrullin-octreotide ( $\text{IC}_{50} = 3 \cdot 10^{-6} \text{ mol/L}$ ). This was in good agreement with the inhibition of growth hormone release from rat anterior pituitary cells (octreotide:  $\text{IC}_{50} = 1.2 \cdot 10^{-10} \text{ mol/L}$ ; 5-(L)-citrullin-octreotide:  $\text{IC}_{50} = 3 \cdot 10^{-6} \text{ mol/L}$ ). Intragastric administration of ethanol to rats resulted in lesions of the gastric mucosa affecting  $18.9 \pm 3.1\%$  of the area of the glandular stomach. Octreotide reduced the area to  $6.4 \pm 1.7\%$  ( $P < 0.05$ ). The dose-response curve was bell-shaped. 5-(L)-citrullin-octreotide was totally devoid of any protective activity (dose range: 0.1 ng/kg to 0.1 mg/kg). The authors further investigated the effect of the two peptides on ethanol-induced microcirculatory stasis and elevated vascular permeability. Ethanol in a concn. of 50% induced an increase in microvascular permeability, measured by the extravasation of the tracer **fluorescein**-isothiocyanate-dextran (mol. wt. 150 000). Pretreatment with octreotide (0.1 ng/kg s.c.) prevented stasis and reduced capillary permeability significantly. 5-(L)-citrullin-octreotide had no effect on ethanol-induced

microcirculatory stasis and elevated vascular permeability in rat gastric mucosa. In summary, very low doses of octreotide have a beneficial effect on ethanol-induced hemorrhagic lesions, microcirculatory stasis and increased capillary permeability. This effect is most likely mediated by **somatostatin receptors**.

L61 ANSWER 24 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:427047 HCAPLUS

DOCUMENT NUMBER: 121:27047

TITLE: Synthesis of a biologically active fluorescent probe for labeling neurotensin receptors

AUTHOR(S): Faure, Marie Pierre; Gaudreau, Pierrette; Shaw, Ivan; Cashman, Neil R.; Beaudet, Alain

CORPORATE SOURCE: Neurobiol. Group, Montreal Neurol. Inst., Montreal, PQ, Can.

SOURCE: J. Histochem. Cytochem. (1994), 42(6), 755-63

CODEN: JHCYAS; ISSN: 0022-1554

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors synthesized a fluorescent deriv. of the tridecapeptide neurotensin (NT), with the aim of providing a new tool for the pharmacol. characterization and anatomical localization of NT receptors in mammalian brain. Fluoresceinylated NT (N.alpha.-fluoresceinyl thiocarbamyl (FTC)-[Glu1]NT) was synthesized using solid-phase methodol. and purified to 99% homogeneity by preparative high-pressure liq. chromatog. (HPLC). Anal. HPLC, acidic and carboxypeptidase Y hydrolysis, and fast atom bombardment-mass spectroscopy confirmed that the purified compd. was selectively labeled on the [Glu1] terminus and that a single FTC moiety was coupled to each mol. of [Glu1]NT. Flow cytometric anal. of the binding of fluo-NT to SN17 septal neuroblastoma cells indicated that the fluorescent deriv. bound neural NT receptors with an affinity comparable to that of monoiodinated NT([125I]-NT). Competition expts. on mouse brain membrane preps. showed fluo-NT to inhibit specific [125I]-NT binding with a coeff. of inhibition (KI) virtually identical to that of the native peptide (0.67 vs 0.55 nM). Conventional epifluorescence and confocal microscopic anal. of specific fluo-NT binding to sections of the rat midbrain revealed a topog. distribution of the bound fluorescent ligand similar to that previously obsd. with autoradiog. using [125I]-NT. However, fluoro-NT provided markedly higher cell resolu. and enabled, in particular, the detection of hitherto unnoted intracytoplasmic receptor clusters. Binding of fluoro-NT to live SN17 hybrid cells indicated that the fluorescent ligand had retained its ability to internalize in vivo and confirmed that this internalization process was both time- and temp.-dependent. In sum, the present study demonstrates that fluo-NT is applicable to both the pharmacol. study of NT binding sites using flow cytometry and to the regional and cellular localization of these sites by conventional epifluorescence and confocal microscopy.

L61 ANSWER 25 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:604556 HCAPLUS

DOCUMENT NUMBER: 117:204556

TITLE: Antagonists that demonstrate species differences in neurokinin-1 receptors

AUTHOR(S): Appell, Kenneth C.; Fragale, Barbara J.; Loscig, Jane; Singh, Saira; Tomczuk, Bruce E.

CORPORATE SOURCE: Dep. Enzymol. Biochem., Sterling Res. Group, Malvern, PA, 19355, USA

SOURCE: Mol. Pharmacol. (1992), 41(4), 772-8  
CODEN: MOPMA3; ISSN: 0026-895X

DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB 125I-Bolton-Hunter-substance P (125I-BH-SP) binding properties of three novel classes of neurokinin-1 (NK-1) receptor antagonists were investigated in tissues derived from humans, guinea pigs, and rats. 125I-BH-SP was shown to bind to a single class of binding sites, with similar dissociation constants,  $K_d$ , in human astrocytoma cells (U-373 MG), human urinary bladder, guinea pig forebrain, guinea pig ileum longitudinal smooth muscle, rat forebrain, and rat duodenum. In each tissue preparation, known peptide agonists and peptide antagonists yielded potencies typical for a NK-1 receptor profile, with little difference in binding properties between the various tissues. However, when the three classes of compounds, heterosteroids, cyanines, and modified peptides, were tested for their ability to displace 125I-BH-SP binding from the NK-1 receptor, very different binding profiles were observed. The heterosteroids were shown to be as much as 3 orders of magnitude more potent in tissues derived from rats than from humans or guinea pigs. A distinct species-dependent structure-activity relationship (SAR) was also observed for this class of compounds. Like the heterosteroids, the cyanines displaced 125I-BH-SP with 10-30-fold higher affinity in rat tissues than in human and guinea pig tissues. However, the SAR generated by the cyanines was comparable in all tissues studied. The modified peptides, on the other hand, were up to 10-100-fold more potent in human and guinea pig than rat tissues, producing a SAR that differed between the various species. No differences in binding properties between central nervous system and peripheral tissues from the same species were seen with these compounds. These results provide evidence for species differences in NK-1 receptors in humans, guinea pigs, and rats. Because it is known that there exists great sequence identity between rat and human NK-1 receptors, it is hypothesized that key amino acid changes or different lipid environments within the transmembrane binding region of the receptor may account for the observed species difference. Furthermore, this study emphasizes that caution is necessary in the choice of species to be used in development programs targeted towards therapeutic entities in the NK-1 receptor antagonist area.

L61 ANSWER 26 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:550938 HCAPLUS

DOCUMENT NUMBER: 115:150938

TITLE: Cell surface-binding sites for progesterone mediate calcium uptake in human sperm

AUTHOR(S): Blackmore, Peter F.; Neulen, Joseph; Lattanzio, Frank; Beebe, Stephen J.

CORPORATE SOURCE: Dep. Pharmacol., East. Virginia Med. Sch., Norfolk, VA, 23501, USA

SOURCE: J. Biol. Chem. (1991), 266(28), 18655-9

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The location of progesterone receptors on the cell surface of human sperm was identified using progesterone immobilized on bovine serum albumin (BSA) (progesterone 3-(O-carboxymethyl)oxime:BSA) as well as progesterone and its 3-O-carboxymethyloxime deriv. Using fluorescence microscopy, BSA-fluorescein isothiocyanate was shown to be excluded from intact sperm, thus validating the use of progesterone 3-(O-carboxymethyl)oxime:BSA to identify cell surface-binding sites for progesterone. The immobilized progesterone and the 3-O-carboxymethyloxime deriv. rapidly increased  $[Ca^{2+}]_i$  and were full agonists, although they were approximately 1.5 orders of magnitude less potent than progesterone. They also displayed an identical time course to increase  $[Ca^{2+}]_i$  as free



progesterone, and the entire increase in  $[Ca^{2+}]_i$  was due to the influx of  $Ca^{2+}$ . This progesterone-mediated response displayed different **steroid receptor** characteristics since the very potent inhibitors of genomic progesterone responses RU 38486 and ZK 98299 were ineffective at inhibiting the progesterone-mediated increase in  $[Ca^{2+}]_i$ . Also the synthetic progestins megestrol, medroxyprogesterone acetate, norgestrel, norethynordrel, norethindrone, R 5020, and cyproterone acetate did not mimic the effects of progesterone to increase  $[Ca^{2+}]_i$ . Thus, a distinct nongenomic cell surface receptor for progesterone exists in human sperm.

L61 ANSWER 27 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:565616 HCAPLUS

DOCUMENT NUMBER: 113:165616

TITLE: Monoclonal and polyclonal antibodies to human progesterone receptor peptide-(533-547) recognize a specific site in unactivated (8S) and activated (4S) progesterone receptor and distinguish between intact and proteolyzed receptors

AUTHOR(S): Traish, Abdulmageed M.; Wotiz, Herbert H.

CORPORATE SOURCE: Sch. Med., Boston Univ., Boston, MA, 02118, USA

SOURCE: Endocrinology (Baltimore) (1990), 127(3), 1167-75

CODEN: ENDOAO; ISSN: 0013-7227

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Three peptides with amino acid sequences corresponding to amino acids 533-547, 597-611, and 765-779 of the human progesterone receptor (hPR) were synthesized. These peptides were conjugated to keyhole limpet **hemocyanin** and injected into mice and rabbits to develop antibodies to hPR. Antibodies to the undenatured form of PR were elicited only by the peptide with amino acid sequence 533-547. Fusion of SP2/0 myeloma cells with spleen cells from mice immunized with this peptide produced several active clones. Rabbit sera from immunized animals produced one antiserum that reacted with the undenatured form of PR. One monoclonal antibody (PR-AT 4.14) and one antiserum (PR-AT533) raised against peptide-(533-547) were characterized. Binding of these antibodies to the undenatured form of PR was demonstrated by anal. of the antibody-receptor complexes on sucrose d. gradients and by immunopptn. techniques. Binding of PR to the antibodies was inhibited by excess peptide. The antibodies did not react with estrogen, glucocorticoid, or androgen receptors, but recognized PR from human breast cancer as well as calf, rabbit, mouse, and rat uteri, indicating that this epitope was conserved among these species. Based on sucrose d. gradient anal. of PR prep'd. and labeled in the presence of proteolysis inhibitors and sodium molybdate, the antibodies bound to a site on the intact undenatured PR, but failed to bind to partially degraded **steroid**-binding form of the **receptor**, suggesting that the antibody-binding domain is at or near a site sensitive to proteolysis.

L61 ANSWER 28 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:530307 HCAPLUS

DOCUMENT NUMBER: 113:130307

TITLE: Development and characterization of monoclonal antibodies to a specific domain of human estrogen receptor

AUTHOR(S): Traish, Abdulmageed M.; Ettinger, Rachel; Kim, Noel; Marshak-Rothstein, Ann; Wotiz, Herbert H.

CORPORATE SOURCE: Sch. Med., Boston Univ., Boston, MA, 02118, USA

SOURCE: Steroids (1990), 55(5), 196-208

CODEN: STEDAM; ISSN: 0039-128X

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Three peptides were synthesized with amino acid sequences identical to those spanning amino acids 201-215, 231-245, and 247-261 of the human estrogen receptor (hER). These peptides were conjugated to keyhole limpet **hemocyanin** and used as immunogens to develop monoclonal antibodies (MoAbs) to hER. Antibody responses were only elicited by the peptide with amino acid sequence 247-261. Splenocytes from immunized mice were used for hybridoma prodn. Of the 7 MoAbs that recognized the native (functional) form of the ER, 4 (MoAbs 16, 33, 114, and 213) recognized the ER with high affinity, as demonstrated by the increased sedimentation coeff. of the antibody-complexed ER in sucrose d. gradients. Antibodies 318, 35, and 36 bound to ER with low affinity since they immunopptd. ER, but the ER-antibody complex appeared to dissoc. on sucrose d. gradients. The high-affinity MoAbs appear to be site-specific since the peptide competed effectively for binding of the receptor by the antibody. The fact that they reacted with ER from human breast cancer and calf, rat, and mouse uterine tissues suggests that this epitope of the receptor is conserved in these species. Although the DNA-binding region appears to be conserved among the various **steroid receptors**, these MoAbs did not recognize the native forms of progesterone, androgen, or glucocorticoid receptors. These MoAbs bound to the KCl-activated 4S ER and heat-transformed 5S ER, suggesting that the antibody-binding site is accessible in the monomeric and dimer forms of ER. The antibodies did not recognize the untransformed 8S ER in the presence of molybdate and without KCl, suggesting that the antibody-binding site in the oligomeric form of ER is inaccessible. The fact that the antibodies did bind to the unoccupied 4S ER was demonstrated by the data obtained with sucrose d. gradient anal. followed by postlabeling of ER with [3H]estradiol. The antibodies bound to ERs with high affinity ( $K_D = 0.4$  to  $1.8$  nM). At a fixed concn. of antibody, ERs ranging from 20 to 1000 fmol were detectable. These MoAbs did not inhibit nuclear or DNA binding of ER in vitro. This can be attributed to the dissocn. of the antibodies from ER when the latter interacts with its acceptor site. These results demonstrate the development of site-specific MoAbs to the native form of the hER using synthetic peptides as immunogens.

L61 ANSWER 29 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:418312 HCAPLUS

DOCUMENT NUMBER: 113:18312

TITLE: Multiple receptors coupled to adenylate cyclase regulate sodium-hydrogen ion exchange independent of cAMP

AUTHOR(S): Ganz, Michael B.; Pachter, Jon A.; Barber, Diane L.

CORPORATE SOURCE: Sch. Med., Yale Univ., West Haven, CT, 06156, USA

SOURCE: J. Biol. Chem. (1990), 265(16), 8989-92

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

AB It was previously detd. that .beta.-adrenergic and **somatostatin receptors** stimulate and inhibit, resp., Na-H exchange independent of changes in cAMP accumulation (Barber, D. L., et al. 1989). Thus, .beta.-adrenergic receptor (.beta.AR) activation of Na-H exchange was examd. in multiple cell types that either endogenously express the .beta.AR or that have been transfected with cDNA of the hamster lung .beta.2AR or the turkey erythrocyte .beta.AR. Exchanger activity was detd. by monitoring intracellular pH in cell populations loaded with the pH-sensitive dye BCECF (2,7-biscarboxyethyl-5(6)-**carboxyfluorescein**). In addn. to the action of the .beta.AR,

activation of PGE1 and parathyroid hormone receptors induced an intracellular alkalinization by stimulating a Na<sup>+</sup>-dependent amiloride-sensitive Na-H exchange. In contrast, activation of D2-dopaminergic receptors induced an intracellular acidification by inhibiting Na-H exchange. .beta.-Adrenergic, PGE1, and parathyroid hormone receptors activated Na-H exchange independent of changes in intracellular cAMP accumulation and independent of a cholera toxin-sensitive stimulatory GTP regulatory protein. Dopaminergic D2 receptors inhibited exchanger activity independent of a pertussis toxin-sensitive inhibitory GTP regulatory protein. Apparently, these receptors are functionally coupled to adenylate cyclase and to Na-H exchange through divergent signaling mechanisms.

L61 ANSWER 30 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:213419 HCAPLUS

DOCUMENT NUMBER: 112:213419

TITLE: Regulation of glucocorticoid receptor expression: I. Use of a specific radioimmunoassay and antiserum to a synthetic peptide of the N-terminal domain

AUTHOR(S): Antakly, Tony; Raquidan, Dolores; O'Donnell, Dajan; Katnick, Leslie

CORPORATE SOURCE: Dep. Anat., McGill Univ., Montreal, PQ, H3A 2B2, Can.

SOURCE: Endocrinology (Baltimore) (1990), 126(4), 1821-8

CODEN: ENDOAO; ISSN: 0013-7227

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To study glucocorticoid receptor (GR) gene expression at the protein level, an antiserum to the GR was produced using a 14 amino acid peptide (14-mer) of amino terminus domain of the human GR, and a simple and specific RIA was established to quantitate both the human and rat GR. The antibody was raised in rabbits to the 14-mer coupled to either BSA or keyhole limpet **hemocyanin**. This antibody immunoblots the Mr = 94,000 bona fide GR in tissue exts. and localizes the GR at the subcellular level by immunocytochem. In addn., cytosolic GR, previously labeled by the affinity ligand, [3H]dexamethasone mesylate, was immunopptd. by the peptide antibody. The 14-mer was iodinated at its tyrosine residue and used in a std. RIA. The binding of the antibody to the 125I-14-mer was displaced by increasing concns. of either the 14-mer (std. curve) pure GR or tissue cytosol contg. native GR. This RIA reliably detects glucocorticoid receptor level at 20-500 fmol/tube in human, rat, and mouse tissues. In 2 well established cell line systems and their subclones (human CEM and in rat hepatoma tissue culture cells transfected or not with GR cDNA) the GR level, as assessed by this RIA, was compared to GR values using the classical radioreceptor or previously published mRNA assays. The relative amt. of GR in wild-type cells and in subclones, as assessed by the novel RIA, was identical to the above-mentioned assays. Using the RIA, the down-regulation of GR level was demonstrated in liver following glucocorticoid administration and its up-regulation following adrenalectomy. This study, which constitutes the 1st description of an RIA for a **steroid receptor** using a synthetic peptide, provides a powerful tool for a standardized, sensitive, and simple assay for the GR in human and animal tissues.

L61 ANSWER 31 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:70282 HCAPLUS

DOCUMENT NUMBER: 112:70282

TITLE: Differential distribution of estrogen and progesterone receptors in rabbit uterus detected by dual immunofluorescence

AUTHOR(S): Zaino, Richard J.; Clarke, Christine L.; Feil, Peter D.; Satyaswaroop, Pondichery G.  
 CORPORATE SOURCE: Milton S. Hershey Med. Cent., Pennsylvania State Univ., Hershey, PA, 17033, USA  
 SOURCE: Endocrinology (Baltimore) (1989), 125(5), 2728-34  
 CODEN: ENDOAO; ISSN: 0013-7227  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The distribution of cells contg. estrogen receptor (ER) and(or) progesterone receptor (PR) was compared in rabbit uterus by immunohistochem. using monoclonal antibodies directed against these receptors. Initial expts. using serial cryostat sections surprisingly revealed the intensity of staining for ER to be inversely proportional to that of PR, as follows: ER, luminal and glandular epithelium > myometrium > stroma; PR, stroma > myometrium > glands > luminal epithelium. Localization was strictly confined to the nuclei of target cells. Single and dual immunofluorescent labeling of ER and PR in cryostat sections was accomplished using fluorochromes with differing emission spectra. Individual fields of dual labeled sections were examd. for red [phycoerythrin (ER)] and green [fluorescein (PR)] fluorescence, with the same distribution as noted by single antibody immunohistochem. Myometrial nuclei displayed fluorescence of equiv. relative intensity for both antibodies. Further, sequential exposure photomicrog. (exposure first in the spectrum of phycoerythrin emission, followed by exposure in the spectrum of fluorescein emission) revealed the presence of occasional stroma cells staining only for PR and some luminal cells staining only for ER. This differential distribution of ER and PR within various cell populations of rabbit is a novel observation and challenges current concepts of receptor regulation. Dual immunofluorescent localization of both ER and PR within individual cells provides a unique perspective from which to investigate the interactive influences of these sex **steroid receptors** at the cellular level.

L61 ANSWER 32 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1988:4501 HCAPLUS

DOCUMENT NUMBER: 108:4501

TITLE: Interleukin-3 modulation of mouse bone marrow derived mast cell receptors for somatostatin

AUTHOR(S): Renold, F. K.; Dazin, P.; Goetzl, E. J.; Payan, Donald G.

CORPORATE SOURCE: Howard Hughes Med. Inst., Univ. California, San Francisco, CA, 94143-0724, USA

SOURCE: J. Neurosci. Res. (1987), 18(1), 195-202

CODEN: JNREDK; ISSN: 0360-4012

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Receptors for somatostatin (SOM)** were identified on mouse bone marrow derived mast cells (MBMMC) and shown to vary in expression with the state of proliferation and differentiation of the MBMMC. Flow cytometric studies of the binding of **fluorescein**-labeled SOM and concurrent analyses of the binding of 125I-labeled SOM demonstrated that the population of MBMMC capable of recognizing SOM specifically is that exhibiting a proliferative response to interleukin-3. The MBMMC that bound SOM reached a maximal no. at 72 h following the addn. of interleukin-3, and were distributed principally in the G2/M phase of the cell cycle. SOM did not influence directly the proliferative responses of MBMMC to interleukin-3. The level of expression of SOM receptors may reflect the state of differentiation of mast cells, as well as detg. the functional sensitivity to the inhibitory effects of SOM.

L61 ANSWER 33 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1987:189303 HCAPLUS

DOCUMENT NUMBER: 106:189303

TITLE: Intracellular localization of the glucocorticoid receptor: evidence for cytoplasmic and nuclear localization

AUTHOR(S): Wikstroem, Ann Charlotte; Bakke, Oddmund; Okret, Sam; Broennegaard, Mikael; Gustafsson, Jan Aake

CORPORATE SOURCE: Karolinska Inst., Huddinge Univ. Hosp., Huddinge, S-141 86, Swed.

SOURCE: Endocrinology (Baltimore) (1987), 120(4), 1232-42

CODEN: ENDOAO; ISSN: 0013-7227

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A monospecific, monoclonal antibody against the glucocorticoid receptor (GR), was used to investigate the intracellular localization of GR both in the presence or absence of ligand. With all fixation methods tested (paraformaldehyde, AcOH in EtOH, Bouin's fixative, and bensochinone in PBS), it was possible to obtain specific GR staining. Fixation with paraformaldehyde was chosen for further studies on the effect of permeabilization with several concns. of Triton X 100 or saponin. A rat Rueber hepatoma (H-4-II-E) and a human uterus carcinoma (NH1K 3025) cell line were used as well as cultured hepatocytes from normal rats. The accessibility of the different cell compartments after fixation and permeabilization was tested for by using antibodies against cellular constituents with known locations (i.e. core-nucleosome proteins and tubulin), in combination with the anti-GR antibody in double immunofluorescence staining expts. The specific GR stain obtained with the indirect peroxidase antiperoxidase technique or with **fluorescein** isothiocyanate-labeled 2nd antibodies was present both in the cytoplasm and in the nucleus. Staining of all cellular compartments was abolished (peroxidase antiperoxidase) or diminished (**fluorescein** isothiocyanate) if the monoclonal antibody was preincubated with a 90% pure GR prepn. These findings are in contrast to recently reported immunocytochem. studies, where a strict nuclear existence of the estrogen and progesterone receptors was reported. Consequently, generalizations with regard to **steroid receptor** localization cannot be made. Furthermore, an in vitro model is described, where the effect of dexamethasone [50-02-2] administration on the localization of receptor staining in H-4-II-E cells can be studied.

L61 ANSWER 34 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1986:491478 HCAPLUS

DOCUMENT NUMBER: 105:91478

TITLE: Formation of a fluorescent glucocorticoid receptor-steroid complex in HTC cell cytosol

AUTHOR(S): Pons, Michel; Robinson, T. E. Joan; Mercier, Louis; Thompson, E. Brad; Simons, S. Stoney, Jr.

CORPORATE SOURCE: Lab. Chem., NIADDK, Bethesda, MD, 20205, USA

SOURCE: J. Steroid Biochem. (1985), 23(3), 267-73

CODEN: JSTBBK; ISSN: 0022-4731

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An intensely fluorescent **rhodamine** deriv. of dexamethasone, Dex-C2-Rho (I) [99143-17-6], was synthesized. I possessed high affinity for hepatoma tissue culture (HTC) cell glucocorticoid receptors in cell-free systems. Whole cell activity and receptor affinity of I were

both much lower, apparently due to problems with cell permeability and(or) metab. A specific, fluorescent **receptor-steroid** complex at concns. as low as  $1 \times 10^{-9}$  M was readily obsd. with crude HTC cell receptors after removal of the free I. This appears to be the 1st report of a fluorescent glucocorticoid **receptor-steroid** complex.

L61 ANSWER 35 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1986:458800 HCAPLUS

DOCUMENT NUMBER: 105:58800

TITLE: Estrogen receptor protein in bone and soft tissue tumors

AUTHOR(S): Weiss, Sharon W.; Langloss, John M.; Shmookler, Barry M.; Malawer, Martin M.; D'Avis, Juan; Enzinger, Franz M.; Stanton, Robert

CORPORATE SOURCE: Dep. Soft Tissue Pathol., Armed Forces Inst. Pathol., Washington, DC, 20306-6000, USA

SOURCE: Lab. Invest. (1986), 54(6), 689-94

CODEN: LAINAW; ISSN: 0023-6837

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Thirty-three histol. diverse bone and soft tissue tumors were analyzed biochem. for the presence of estrogen receptor protein (ERP) and progesterone receptor by means of a conventional, com. available, steroid-binding assay (dextran-coated charcoal method) on fresh frozen tissue. These results were compared with anal. of ERP by using a specific monoclonal antibody both in an enzyme immunoassay (EIA) and on frozen tissue sections by using immunohistochem. procedures. Frozen tissue sections were also examd. for the presence of estrogen and progesterone **receptors** using **fluorescein-labeled steroids**.

Six of the 33 tumors (18%) contained low levels of ERP ranging from 19-73 fmol/mg as detd. by the dextran-coated charcoal method. The remaining 27 cases contained no (<10 fmol/mg) ERP. The ERP-pos. group included a fibromatosis, leiomyosarcoma, liposarcoma (2 cases), neural sarcoma, and a synovial sarcoma. Four were high grade sarcomas, and 2 were low grade sarcomas. There was excellent agreement between the ERP levels detd. by the dextran-coated charcoal method and those detd. by EIA. ERP could not be demonstrated immunohistochem. on frozen tissue sections of the tumors even though it could be demonstrated in breast carcinomas serving as pos. controls. The failure of the immunohistochem. technique may be related to the low levels of ERP in these tumors and the difficulty of detecting antigen at threshold levels. Cytochem. localization of **receptor** protein employing **fluoresceinated steroids** did not correlate with cytosolic ERP as detd. by EIA or the dextran-coated charcoal method. Moreover, the high level of background fluorescence gave rise to a significant amt. of intraobserver and interobserver variation.

L61 ANSWER 36 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1986:404397 HCAPLUS

DOCUMENT NUMBER: 105:4397

TITLE: Binding of **fluorescein isothiocyanate** conjugated lectins to MXT mouse mammary neoplasm and their relation to **steroid receptor** status

AUTHOR(S): Kiss, Robert; Lenglet, Georges; Danguy, Andre

CORPORATE SOURCE: Fac. Med., Univ. Libre Bruxelles, Brussels, 1000, Belg.

SOURCE: Anticancer Res. (1986), 6(2), 209-13

CODEN: ANTRD4; ISSN: 0250-7005

DOCUMENT TYPE: Journal

LANGUAGE: English

AB As previous studies have suggested a hormone dependence of binding sites for peanut agglutinin (PNA) in mammary neoplasms, this feature has been thought to be correlated to steroid receptor status. The present investigation was undertaken on a well-established ovarian-dependent cancer model in order to check this hypothesis. Sections of primitive tumor transplants as well as of tumors induced in vivo by injection of cell clones were analyzed with the use of 3 fluorescent lectins. The lectin binding sites were evaluated semi-quant. and compared with estrogen and progesterone receptor levels. Using non-parametric statistical tests, the results revealed a strong correlation between the expression of PNA binding sites and steroid receptor status, but only in primitive tumor transplants. No such correlation was obsd. in tumors induced in vivo, by injection of cell clones. No correlation between the steroid receptor status and the 2 other lectins (Concanavalin A and Dolichos biflorus) was obsd. Apparently, PNA can be used as a valuable histochem. tool in steroid hormone dependence studies.

L61 ANSWER 37 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1985:612528 HCAPLUS

DOCUMENT NUMBER: 103:212528

TITLE: Biochemical and histochemical analysis of steroid hormone binding sites in human primary breast cancer

AUTHOR(S): Janssens, Jaak P.; Pylyser, Kris; Bekaert, Jan; Roelens, Jan; Stuyck, Jacques; Dekeyser, Luc J.; Lauweryns, Jozef M.; De Loecker, William

CORPORATE SOURCE: Afdeling Biochem., Kathol. Univ. Leuven, Louvain, B-3000, Belg.

SOURCE: Cancer (Philadelphia) (1985), 55(11), 2600-11

CODEN: CANCAR; ISSN: 0008-543X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mammary carcinoma tissue from 514 primary breast cancer patients were all biochem. and histochem. analyzed for both estrogen receptors and progesterone receptors. The dextran-coated charcoal method measured the ER and PR as defined by Scatchard anal., ligand competition expts., and target organ specificity. The ligands, estradiol-6-carboxymethyloxime-bovine serum albumin (BSA)-**fluorescein** isothiocyanate and hydroxyprogesteronehemisuccinate-BSA-**tetramethylrhodamine** isothiocyanate, used for histochem., did not bind to either ER or PR and were mainly bound to the membrane fraction of isolated breast cancer cells. Fluorescence was not specifically inhibited by estrogens or progestogens. In addn., estrogenic always coincided with progestogenic fluorescence. The binding of the **fluorescein** compds. to tissue slides depended on the large steroid hormone substitution on the BSA mol. Clin. parameters known to be related to ER and PR did not correlate with the histochem. results. The observations indicated the impossibility of specific **steroid receptor** detection by the histochem. method. Therefore, at present, evaluation of hormone dependency and prognosis in human breast cancer cannot be based on this approach.

L61 ANSWER 38 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1985:90173 HCAPLUS

DOCUMENT NUMBER: 102:90173

TITLE: Fluorescent ligands do not discriminate between androgen receptor and/or oestrogen receptor-positive and -negative human tumor cells

AUTHOR(S): Berns, Els M. J. J.; Blankenstein, Rien A.; De Goey, Ton F. P. M.; Bolt-de Vries, Joan; Mulder, Eppo; Van

der Molen, Henk J.  
 CORPORATE SOURCE: Med. Fac., Erasmus Univ., Rotterdam, 3000 DR, Neth.  
 SOURCE: Adv. Urol. Oncol. Endocrinol., Proc. Congr. Eur. Soc.  
 Urol. Oncol. Endocrinol., 3rd (1984),  
 Meeting Date 1983, 15-25. Editor(s): Bracci, Ulrico;  
 Di Silverio, Franco. ACTA MED. Ed. Congr. s.r.l.:  
 Rome, Italy.  
 CODEN: 52VUA6  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

AB Androgens and estrogens coupled via bovine serum albumin (BSA) or a hemisuccinate bridge to fluorescent ligands were evaluated for reliable **steroid receptor** localization in human tumor cells. Testosterone 17.beta.-hemisuccinate was coupled via BSA to FITC or directly to **fluoresceinamine**. Estradiol 6-carboxymethyloxime was coupled to FITC by BSA. Estradiol 17-hemisuccinate was coupled to **fluoresceinamine**, and dehydrotestosterone 17.beta.-hemisuccinate was coupled to **fluoresceinamine**. Human prostate adenocarcinoma cells (PC-93 and EB-33), human breast cancer cells (MCF-7), and human uterine cervix carcinoma cells (NHK-3025) were stained with these ligands and their ability to discriminate androgen and(or) estrogen receptors was detd. and compared to biochem. ests. of receptor d. The fluorescent ligands stained both receptor-pos. and receptor-neg. cells. Androgen and estrogen receptor could not be visualized by this method. Fluorescence was apparently due to low-affinity binding sites but the presence of these sites was not correlated to the presence or absence of androgen or estrogen receptors.

L61 ANSWER 39 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1984:6934 HCAPLUS

DOCUMENT NUMBER: 100:6934

TITLE: Use of high-performance liquid chromatography in the evaluation of the synthesis and binding of **fluorescein-linked steroids** to estrogen **receptors**

AUTHOR(S): Lonsdorfer, Michael; Clements, Neil C., Jr.; Wittliff, James L.

CORPORATE SOURCE: Health Sci. Cent., Univ. Louisville, Louisville, KY, 40292, USA

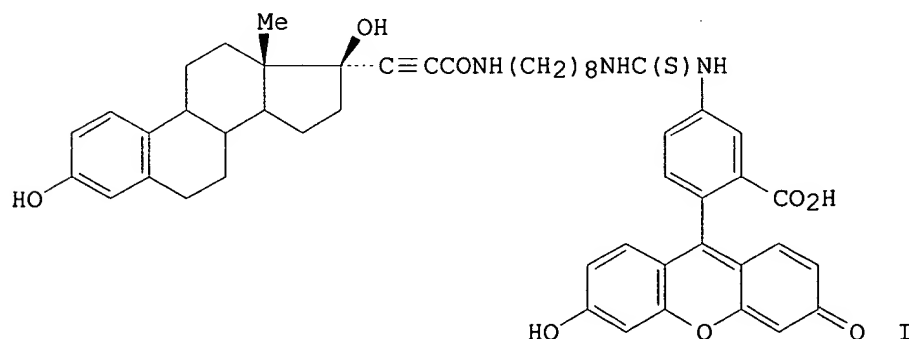
SOURCE: J. Chromatogr. (1983), 266, 129-39

CODEN: JOGRAM; ISSN: 0021-9673

DOCUMENT TYPE: Journal

LANGUAGE: English

GI





AB Fluorescein-linked estrogen I was prepd. as a non-invasive, non-radiochem. means of detecting the levels and distribution of estrogen receptors in histol. preps. of breast and endometrium. 17.alpha.-Ethinylestradiol-21-carboxylic acid was coupled via octane-1,8-diamine to fluorescein-isothiocyanate to give I. High-performance liq. chromatog. on preparative reversed-phase C18 columns was used to purify the final product. Using cytosolic receptor preps. from bovine uterus and human uterus and breast cancer, the binding of I was detd. by competition analyses to have a Kd value of 10<sup>-8</sup> M. High- and low-mol.-wt. forms of estrogen receptors were sepd. by high-performance size-exclusion chromatog. Specific binding of radio labeled estradiol-17.beta. to these forms was inhibited in the presence of I, indicating assocn. with the fluorescein-linked steroid.

L61 ANSWER 40 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:101425 HCAPLUS

DOCUMENT NUMBER: 98:101425

TITLE: Studies with steroid-fluorescein conjugates on estrogen target tissues

AUTHOR(S): Joyce, B. G.; Nicholson, R. I.; Morton, M. S.; Griffiths, K.

CORPORATE SOURCE: Tenovus Inst. Cancer Res., Welsh Natl. Sch. Med., Heath/Cardiff, CF4 4XX, UK

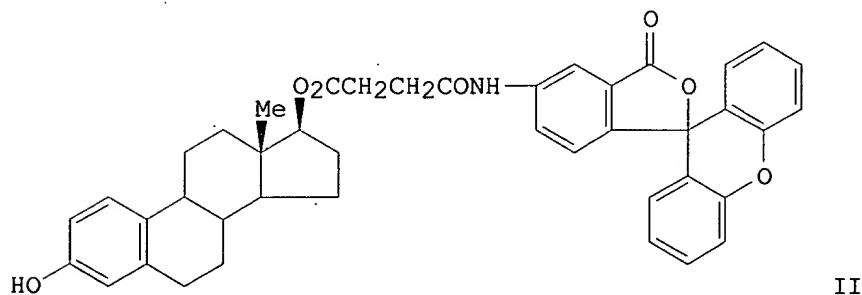
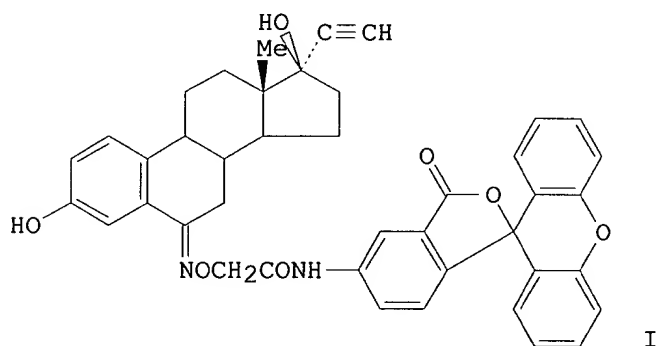
SOURCE: Eur. J. Cancer Clin. Oncol. (1982), 18(11), 1147-55

CODEN: EJCODS; ISSN: 0277-5379

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB Steroid-fluorescein amine (FA) and steroid-bovine serum albumin-fluorescein-isothiocyanate conjugates, including 6-O-carboxymethyloximeethynylestradiol-FA (I) [84872-63-9] and 17.beta.-estradiol hemisuccinate-FA (II) [84872-64-0], were prepd. and their abilities to bind to estrogen receptors were assessed in competitive binding studies. The binding of all the fluorescent conjugates to uterine cytosol proteins was low when compared with either estradiol [50-28-2] or diethylstilbestrol [56-53-1]. A comparative study was carried out to assess the relation between estrogen receptor content, detd. biochem., and histochem. localization of the estrogen binding components on thin sections of rat uteri, DMBA-induced mammary tumors, and human breast tumor tissue taken at mastectomy. In thin sections of tissue, all of these conjugates appear to bind not to the classical estrogen receptor moiety but rather to other estrogen-binding proteins.

L61 ANSWER 41 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1982:417581 HCAPLUS

DOCUMENT NUMBER: 97:17581

TITLE: Inhibition of steroid-mediated induction of .delta.-aminolevulinic acid synthase by 2-diethylaminoethyl-2,2-diphenylvalerate hydrochloride (SKF 525-A)

AUTHOR(S): Lane, Stanley E.; Gidari, Anthony S.; Levere, Richard D.

CORPORATE SOURCE: Div. Biomed. Sci., Meharry Med. Coll., Nashville, TN, 37208, USA

SOURCE: Biochim. Biophys. Acta (1982), 716(2), 117-25

CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The inhibition of the steroid-mediated induction of .delta.-aminolevulinic acid synthase [9037-14-3], the rate-limiting enzyme in hepatic **porphyrin**-heme biosynthesis, by SKF 525-A [62-68-0] was studied in cultured chick embryo liver cells. The formation of **porphyrins** in response to cyproterone [2098-66-0], a synthetic steroid, was inhibited in a time-dependent manner by SKF 525-A, an inhibitor of several drug-metabolizing enzyme systems. This action is a result of an inhibitory effect of SKF 525-A on the cyproterone-mediated induction of .delta.-aminolevulinic acid synthase; SKF 525-A also inhibited the induction of the enzyme by the naturally occurring 5.beta.-H steroids etiocholanolone [53-42-9] and 5.beta.-pregnan-3.beta.-ol-20-one [128-21-2]. Tests with [3H]etiocholanolone provided evidence that this inhibition was not assocd. with either decreased uptake or an altered metab. of the steroid. Moreover, .apprx.4-6 fold more radioactivity was assocd. with [3H]etiocholanolone-treated cells cultured in the presence of SKF 525-A than with those cultured in its absence. Alternative mechanisms for the induction of .delta.-aminolevulinic acid synthase by steroids are proposed which do not require the interaction of **steroid-receptor** complex with the genome.

L61 ANSWER 42 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1982:193551 HCAPLUS

DOCUMENT NUMBER: 96:193551

TITLE: Cytochemical analysis of human breast cancer with fluorescent sex-steroid conjugates. Comparison with biochemical assessment of estrogen receptors

AUTHOR(S): Danguy, A.; Leclercq, G.; Pattyn, G.; Devleeschouwer, N.; Pasteels, J. L.; Heuson, J. C.

CORPORATE SOURCE: Lab. Histol., Fac. Med., Brussels, 1000, Belg.

SOURCE: Anticancer Res. (1981), 1(6), 361-6  
CODEN: ANTRD4

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human mammary cancer cells exhibited cytoplasmic fluorescence labeling when treated with the reagents 17.beta.-estradiol-6-carboxymethyloxime-bovine serum albumin-**fluorescein** isothiocyanate or 11.alpha.-hydroxyprogesterone hemisuccinate-bovine serum albumin-**tetramethylrhodamine** isothiocyanate; the same reagents without their steroid components did not stain the cells. However, the addn. of steroids by themselves did not lessen the intensity of staining, both estrogen receptor-pos. and estrogen receptor-neg. cell lines were stained, the estrogen-contg. reagent had a very low binding affinity for estrogen receptors (as measured by competitive inhibition for the binding of [3H]estradiol), and histochem. detns. of the frequency of occurrence of steroid-pos. cells showed no correlation with results detd. by biochem. methods. Thus, the significance of the staining method for assessing **steroid receptor** in human breast cancer is not known.

L61 ANSWER 43 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1981:58587 HCAPLUS

DOCUMENT NUMBER: 94:58587

TITLE: Histochemical detection of steroid hormone receptors in the human prostate

AUTHOR(S): Pertschuk, Louis P.; Zava, David T.; Tobin, Ellis H.; Brigati, David J.; Gaetjens, Eric; Macchia, Richard J.; Wise, Gilbert J.; Wax, Harry S.; Kim, Dong S.

CORPORATE SOURCE: Sch. Med., State Univ. New York, Brooklyn, NY, 11203, USA

SOURCE: Prog. Clin. Biol. Res. (1979), 33(Prostate Cancer Horm. Recept.), 113-32  
CODEN: PCBRD2; ISSN: 0361-7742

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The presence of estrogen and androgen receptor proteins in human prostatic carcinoma and benign prostatic hyperplasia was identified histochem. using estradiol 17.beta.-hemisuccinate and testosterone 17.beta.-hemisuccinate covalently linked to fluoresceinated bovine serum albumin. The specificity of the histochem. assays for these receptors was indicated by the high correlation of results with those of biochem. anal. and by competitive binding studies using MCF-7 cells as substrate. The major disadvantage of the histochem. technique, that of quantification, might be circumvented by microfluorometry.

L61 ANSWER 44 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1980:634428 HCAPLUS

DOCUMENT NUMBER: 93:234428

TITLE: Synthesis of fluorescein-labeled steroid hormone-albumin conjugates for the fluorescent histochemical detection of hormone receptors

AUTHOR(S): Gaetjens, Eric; Pertschuk, Louis P.

CORPORATE SOURCE: Dep. Pathol., State Univ. New York, Brooklyn, NY, 11203, USA

SOURCE: J. Steroid Biochem. (1980), 13(8), 1001-3  
CODEN: JSTBBK; ISSN: 0022-4731

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The prepn. is described of fluorescein-labeled conjugates of estradiol 17.beta.-hemisuccinate, testosterone 17.beta.-hemisuccinate, and progesterone 11.alpha.-hemisuccinate with bovine serum albumin (covalently

coupled). The preps. contained <1% free hormone or fluorescein. These conjugates can be used for the fluorescent histochem. detection of estrogen, androgen, and progesterone receptors in cancer tissue specimens.

L61 ANSWER 45 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1980:617594 HCAPLUS

DOCUMENT NUMBER: 93:217594

TITLE: Cytochemical agents and methods for the detection of steroid hormone receptors in human tissues

INVENTOR(S): Lee, Sin Hang

PATENT ASSIGNEE(S): USA

SOURCE: S. African, 45 pp.

CODEN: SFXAB

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ZA 7900566	A	19800326	ZA 1979-566	19790209 <--
PRIORITY APPLN. INFO.:			US 1978-876564	19780210 <--
AB Cytochem. agents and methods useful for the investigation of estrogen and (or) progesterone and other hormone binding of cancer cells is described. Sections of mammary carcinoma were removed, frozen, and unfixed sections 14 .mu. thick were mounted and rehydrated with a brief rinse in phosphate buffered saline (PBS). Blocks frozen at -20.degree. were unsuitable, but those at 2-5.degree. preferred. The specimen was then coated with a fluorescent estradiol conjugate and incubated at room temp. for 2 h. After washing in PBS the specimen was examd. under a fluorescence microscope. The presence of cellular fluorescence is interpreted as evidence of the presence of estrogen receptors. A fluorescein isothiocyanate (FITC)-bovine serum albumin (BSA) complex with a high FITC-BSA was prepd. by mixing 1 g BSA with 1 g FITC on 10% celite for 4 h at room temp. The celite was removed and the FITC-BSA complex was chromatographed on Sephadex G-25 and then dialyzed to remove unreacted FITC. The av. fluorescein/protein ratio was 11.2. An aliquot of FITC-BSA contg. 200 mg protein was mixed with 200 mg carbodiimide, 200 mg 17.beta.-estradiol-6-(O-carboxymethyl)oxime, and buffer for 20 h. The conjugate was then dialyzed against H2O and PBS, centrifuged, preserved with NaN3 and used to stain for estrogen receptor.				

L61 ANSWER 46 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1980:600592 HCAPLUS

DOCUMENT NUMBER: 93:200592

TITLE: Cytochemical agents and methods for the detection of steroid hormone receptors in human tissues

INVENTOR(S): Lee, Sin H.

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 947,700, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4215102	A	19800729	US 1979-1205	19790105 <--

IL 56467	A1	19820430	IL 1979-56467	19790119 <--
AU 7943676	A1	19790816	AU 1979-43676	19790125 <--
AU 529917	B2	19830623		
CA 1129758	A1	19820817	CA 1979-320580	19790131 <--
EP 3583	A1	19790822	EP 1979-100329	19790205 <--
EP 3583	B1	19811202		
R: BE, CH, DE, FR, GB, IT, LU, NL, SE				
JP 54119993	A2	19790918	JP 1979-14888	19790210 <--
JP 02002104	B4	19900116		
PRIORITY APPLN. INFO.:			US 1978-876564	19780210 <--
			US 1978-947700	19780929 <--
			US 1979-1205	19790105 <--

AB Fluorescent staining reagents and methods are described for detecting estrogen and progesterone receptors in sections from breast carcinoma for evaluation of potential endocrine therapy of the patient. A fluorescein isothiocyanate (FITC)-bovine serum albumin (BSA) complex with an av. fluorescein/protein rates of 11.2 was prepd. and conjugated with 17.beta.-estradiol-6-(O-carboxymethyl)oxime (I). FITC-BSA complex (200 mg protein) in a 0.05M phosphate buffer was mixed with I (200 mg) dissolved in 6 mL dioxane, and 5 mL H<sub>2</sub>O in the presence of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (200 mg) and sufficient phosphate buffer to 21 mL for 20 h at room temp. The FITC-BSA-I conjugate was then dialyzed against H<sub>2</sub>O and phosphate buffered saline and centrifuged. The conjugate was used in dild. form (equiv. to 0.5 .mu.M FHC/mL) to stain unfixed frozen tissue sections. Fixation in cold acetone or buffered formaldehyde or glutaraldehyde eliminates cellular estrogen binding. Strongly pos. estrogen receptor cells were characterized by heavy fluorescent deposits of FITC-BSA-I in the cytoplasm and to a lesser extent in the nuclei.

L61 ANSWER 47 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1980:563901 HCAPLUS

DOCUMENT NUMBER: 93:163901

TITLE: Estrogen receptor cytochemistry by fluorescent estrogen

AUTHOR(S): Nenci, I.; Dandliker, W. B.; Meyers, C. Y.; Marchetti, E.; Marzola, A.; Fabris, G.

CORPORATE SOURCE: Ist. Anat. Patol., Univ. Ferrara, Ferrara, 44100, Italy

SOURCE: J. Histochem. Cytochem. (1980), 28(10), 1081-8

CODEN: JHCYAS; ISSN: 0022-1554

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 1-(N)-**Fluoresceinylestrone** thiosemicarbazone (17FE), a recently synthesized **fluorescein**-labeled estrogen, interacts with estrogen-target cells like the native hormone and visualizes the uptake, transport, and distribution of estrogen in intact target cells. Moreover, estrogen binding sites are traced by 17FE in cryostat sections of estrogen target tissues as well. Cell and tissue 17FE binding sites fulfill the accepted criteria for specific estrogen **receptors** (finite binding capacity, high affinity, **steroid** and tissue specificity). This fluorescent probe allows estrogen receptors to be studied in a wide variety of cell and tissue preps. under varying conditions of physiologic and pathophysiologic interest.

L61 ANSWER 48 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1980:528195 HCAPLUS

DOCUMENT NUMBER: 93:128195

TITLE: **Receptor** binding of **fluorescein**

-labeled **steroids**  
 AUTHOR(S): Daxenbichler, G.; Grill, H. J.; Domanig, R.; Moser, E.; Dapunt, O.  
 CORPORATE SOURCE: Dep. Obstet. Gynecol., Univ. Innsbruck, Innsbruck, Austria  
 SOURCE: J. Steroid Biochem. (1980), 13(5), 489-93  
 CODEN: JSTBBK; ISSN: 0022-4731  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Fluorescent derivs. of 17.beta.-estradiol (I), deoxycorticosterone (II), and prednisolone (III) were synthesized by coupling I-hemisuccinate, II-21-hemisuccinate, and III-21-hemisuccinate to N-**fluoresceinyl**-5,N'-(6-amino)hexylthiourea. The long chain of C and N atoms between the steroid and **fluorescein** was introduced to avoid steric hindrance of the **steroid-receptor** interaction. The KD values for binding of I and I-**fluorescein**-conjugate to rabbit uterine cytosol receptors were 0.8 and 1.5 nM, resp., and those for binding of progesterone and II-**fluorescein**-conjugate to progesterone receptors were 2.3 nM and 9.7 nM, resp. The KD values for binding of dexamethasone and III-**fluorescein** conjugate to rabbit liver glucocorticoid receptors were 3.4 and 7.3 nM resp.

L61 ANSWER 49 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1980:140828 HCAPLUS  
 DOCUMENT NUMBER: 92:140828  
 TITLE: Steroid-cell interactions revealed by immunological probes and electron microscopy  
 AUTHOR(S): Nenci, Italo; Fabris, Guidalberto; Marzola, Andrea; Marchetti, Elisabetta  
 CORPORATE SOURCE: Inst. Anat. Pathol., Univ. Ferrara, Ferrara, Italy  
 SOURCE: Pharmacol. Modulation Steroid Action (1980), 99-110. Editor(s): Genazzani, Enrico; Di Carlo, Francesco; Mainwaring, W. Ian P. Raven: New York, N. Y.  
 CODEN: 42SRA5  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English

AB The specificity of estradiol [50-28-2] binding by human breast tumor cells was studied by an immunofluorescence assay (Nenci et al, 1976-8) in which **fluorescein** was substituted by horseradish peroxidase and electron microscopy. In cells incubated with estradiol at 4.degree., the antibody techniques showed that estradiol binding was first bound to components of the plasma membrane and then by cytoplasmic ribosomes and(or) polyribosomes. At 20.degree. a max. perinuclear concn. of the bound hormone was obsd. Electron microscopy revealed this to be with particles in contact with the nuclear membrane. The morphol. and size of these particles was discussed. Penetration of material into the nucleoplasm was obsd. and the mechanism was discussed. **Steroid-receptor** complexes at the nucleolar level were also mentioned.

L61 ANSWER 50 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1980:89531 HCAPLUS  
 DOCUMENT NUMBER: 92:89531  
 TITLE: Steroid-albumin conjugate interaction with steroid-binding proteins  
 AUTHOR(S): Rao, B. Ramanath; Patrick, Timothy B.; Sweet, Frederick  
 CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, 63110, USA  
 SOURCE: Endocrinology (Baltimore) (1980), 106(1), 356-62

CODEN: ENDOAO; ISSN: 0013-7227

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of progesterone (I)-bovine serum albumin (BSA) conjugates were synthesized by precisely controlling the molar ratios in the reaction mixts. of hemisuccinyloxyprogesterone, isobutyl chloroformate, and BSA. I was conjugated to BSA via the 2.alpha., 11.alpha., or 21 positions. 17.beta.-Estradiol (II) was conjugated through a 6-carboxymethyloxime side chain to BSA. An addnl. series of steroid-BSA conjugates was prepd. in which **fluorescein** was attached to the BSA portion. All of the conjugates were tested for binding to rabbit uterine cytoplasmic I and estrogen receptors using charcoal adsorption and sucrose d.-gradient techniques. I-BSA and II-BSA conjugates competed against I-3H and II-3H for the appropriate receptor proteins, but hemisuccinyloxyprogesterones and 6-carboxymethyloximino-II did not compete against **steroid** hormones for the appropriate **steroid receptors**. 21-I-BSA in the I-BSA series showed the highest degree of competition against I-3H for the I receptor. The max. competitive activity of 21-I-BSA was obsd. for a steroid-to-BSA ratio of 6:1. Substrate activity of I-BSA conjugates with the 20.beta.-hydroxysteroid dehydrogenase (EC 1.1.1.53) showed that activity is maximal with I linked to BSA via the 21 position, and it varied with the steroid-to-BSA ratio. The highest substrate activity for the 21-I-BSA series was obtained with a I-to-BSA ratio of 6:1. The presence of a nonsteroid mol. on BSA did not influence the interaction of the **steroid** moiety of the conjugate with **receptor** protein, as shown by competition studies with 21-I-BSA-**fluorescein** or II-BSA-**fluorescein** conjugates with I or estrogen receptor. Binding activity was due solely to the conjugates and not to steroid released from BSA by hydrolysis of a steroid ester linkage. Steroid covalently linked to BSA retained the ability to interact with the receptor and enzyme. Steroid-BSA-**fluorescein** conjugates have the potential for detecting steroid target tissues and cells.

L61 ANSWER 51 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1979:471271 HCAPLUS

DOCUMENT NUMBER: 91:71271

TITLE: Histochemistry of steroid receptors in prostatic diseases

AUTHOR(S): Pertschuk, Louis P.; Zava, David T.; Gaetjens, Eric; Macchia, Richard J.; Wise, Gilbert J.; Kim, Dong S.; Brigati, David J.

CORPORATE SOURCE: Downstate Med. Cent., State Univ. New York, Brooklyn, NY, 11203, USA

SOURCE: Ann. Clin. Lab. Sci. (1979), 9(3), 225-9

CODEN: ACLSCP; ISSN: 0095-8905

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tissues obtained from 55 men with prostatic disease were assayed for estrogen and androgen receptors by a newly developed histochem. technique utilizing fluorescein isothiocyanate-bovine serum albumin conjugates with .beta.-estradiol 17-hemisuccinate or .beta.-testosterone 17-hemisuccinate. The material studied consisted of 45 specimens of benign nodular prostatic hyperplasia and 10 specimens of prostatic adenocarcinoma. The results obtained were compared to those of parallel biochem. assays in 17 cases and successfully correlated in 85%. The new procedure is accurate, allowing for the detection of receptor in cytoplasm and (or) nucleus and evaluation of receptor heterogeneity.

L61 ANSWER 52 OF 52 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1976:174900 HCAPLUS

DOCUMENT NUMBER: 84:174900  
 TITLE: Biochemical and immunological studies of h-proteins from the liver of animals distinguished by their sensitivity to carcinogenic azo dyes  
 AUTHOR(S): Kaledin, V. I.  
 CORPORATE SOURCE: USSR  
 SOURCE: Itogi Nauchn. Rab., Akad. Nauk SSSR, Sib. Otd., Inst. Tsitol. Genet. (1974), Meeting Date 1973, 30-1. Akad. Nauk SSSR, Sib. Otd., Inst. Tsitol. Genet.: Novosibirsk, USSR.  
 CODEN: 32QYA5  
 DOCUMENT TYPE: Conference  
 LANGUAGE: Russian

AB Radial immunodiffusion expts. showed that only 1 of 2 h-protein fractions isolated from rat and mouse liver reacted with **azo dyes** and benzidine [92-87-5]. Factors which inhibited the carcinogenic action of **azo dyes** increased the h-protein content of the liver, whereas factors stimulating hepatocarcinogenesis decreased the h-protein levels of the liver. Expts. with sex hormones and hydrocortisone suggest that the liver h-proteins are bound to **steroid hormone receptors** and that the carcinogens decrease the functioning of these proteins and disrupt the hormonal regulation of liver cells.



#3 of your request

CEPERLEY 09/898,885

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L15 24 SEA FILE=REGISTRY ABB=ON PLU=ON (AZIDE/CN OR "AZIDE (H(N3)21-  
)/CN OR "AZIDE (H(N3)21-), TETRAPHENYLPHOSPHONIUM"/CN OR  
"AZIDE (N3-)/CN OR "AZIDE DIBENZYLDMETHYLAMMONIUM"/CN OR  
"AZIDE ION"/CN OR "AZIDE ION(1-)/CN OR "AZIDE RADICAL"/CN OR  
"AZIDE(1-)/CN OR "AZIDE, COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3  
-OXOOCTADECAXOCTADECANADATE(10-) (1:1)/CN OR "AZIDE,  
COMPD. WITH HEXA-.MU.-OXOEICOSA-.MU.3-OXOOCTADECAXOCTADECAN  
ADATE(13-) (1:1)/CN OR "AZIDE, LABELED WITH NITROGEN-15"/CN  
OR "AZIDE, MONOHYDRATE"/CN OR AZIDE-1-15N/CN OR AZIDE-15N2/CN  
OR AZIDE-15N3/CN OR AZIDE-2-15N/CN OR AZIDIAMANTANE/CN OR  
"AZIDIC ACID"/CN OR AZIDIN/CN OR AZIDIN-NAGANIN/CN OR AZIDINE/C  
N OR "AZIDINE FAST SCARLET 4BS"/CN OR "AZIDINE FAST SCARLET  
7BS"/CN OR "AZIDINE FAST SCARLET GGS"/CN OR "AZIDINE YELLOW  
5G"/CN OR AZIDIOL/CN OR AZIDITHION/CN OR AZIDO/CN OR "AZIDO  
RADICAL"/CN)

L16 16 SEA FILE=REGISTRY ABB=ON PLU=ON "AZIDE" AND L15

L18 545 SEA FILE=REGISTRY ABB=ON PLU=ON "AZID"

L19 3867 SEA FILE=HCAPLUS ABB=ON PLU=ON L16

L20 36392 SEA FILE=HCAPLUS ABB=ON PLU=ON L18

L21 141428 SEA FILE=HCAPLUS ABB=ON PLU=ON (N3 OR ?AZID? OR NITRENE OR  
SINGLET OXYGEN)

L22 2611 SEA FILE=HCAPLUS ABB=ON PLU=ON DYE(L) (L19 OR L20 OR L21)

L23 191092 SEA FILE=HCAPLUS ABB=ON PLU=ON ?CYANIN? OR ?RHODAMIN? OR  
?PHENOXAZIN? OR ?PHENOTHIZIN? OR ?PHENOSELENAZIN? OR ?FLUORESC  
IN? OR ?PORPHYRIN? OR ?BENZOPORPHYRIN? OR ?SQUARAIN? OR  
?CORRIN? OR ?COROCONIUM? OR AZO(W)DYE OR METHIN?(W)DYE OR  
INDOLENIUM(W)DYE

L24 586 SEA FILE=HCAPLUS ABB=ON PLU=ON L22(L)L23

L25 1965 SEA FILE=HCAPLUS ABB=ON PLU=ON RECEPTOR(3A) (SOMATOSTATIN OR  
BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN  
OR STEROID) (3A) BIND?

L26 0 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 AND L25

L27 13956 SEA FILE=HCAPLUS ABB=ON PLU=ON RECEPTOR(5A) (SOMATOSTATIN OR  
BACTERIOENDOTOXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN  
OR STEROID)

L29 163257 SEA FILE=HCAPLUS ABB=ON PLU=ON (SOMATOSTATIN OR BACTERIOENDOT  
OXIN OR NEUROTENSIN OR BOMBESIN OR CHOLESYSTEKNIN OR STEROID)

L30 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L24

L31 90 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L23

L32 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L21 AND L31

L33 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 OR L32

L34 88 SEA FILE=HCAPLUS ABB=ON PLU=ON L27 AND L21

L35 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L34 AND L23

L38 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L29

L39 53 SEA FILE=HCAPLUS ABB=ON PLU=ON L27(L)L23

L40 55 SEA FILE=HCAPLUS ABB=ON PLU=ON (L19 OR L20 OR L21) (L)L27

L44 318 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPOCRELLIN?

L45 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L44

L46 65735 SEA FILE=HCAPLUS ABB=ON PLU=ON HYPOCRELLIN? OR AZO OR  
METHINE OR INDOLENIUM

L47 429 SEA FILE=HCAPLUS ABB=ON PLU=ON L22 AND L46

L48 429 SEA FILE=HCAPLUS ABB=ON PLU=ON L47 AND DYE

L50 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L48 AND L29

L57 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L39 AND PATENT/DT

L58 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L57 AND PRD<20010307

L59 44 SEA FILE=HCAPLUS ABB=ON PLU=ON L39 NOT L57

L60 43 SEA FILE=HCAPLUS ABB=ON PLU=ON L59 AND PD<20010307

L61 52 SEA FILE=HCAPLUS ABB=ON PLU=ON L58 OR L60

CEPERLEY 09/898,885

L62	3	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L40(L)CONJUGAT?
L63	3	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L40 AND CONJUGAT?
L64	24	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L40 AND (COVALENT? OR BOND? OR LINK?)
L65	27	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	(L62 OR L63 OR L64)
L72	186373	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	NECROSIS OR APOPTOSIS OR PHOTOSENIT? OR PHOTODYNMIC? OR SINGLET OXYGEN OR PHOTOTHERAP? OR TYPE(W) (1 OR 2)
L76	154	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L72(5A) (AZIDE OR NITRENE)
L77	27	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L76 AND (L23 OR L26)
L78	27	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L77 NOT (L65 OR L61 OR L50 OR L45 OR (L32 OR L33) OR L38 OR L35)

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L78 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:780046 HCAPLUS

DOCUMENT NUMBER: 136:158662

TITLE: Comparative photosensitized transformation of polychlorophenols with different sulfonated **metallophthalocyanine** complexes in aqueous medium

AUTHOR(S): Ozoemena, Kenneth; Kuznetsova, Nina; Nyokong, Tebello  
 CORPORATE SOURCE: Department of Chemistry, Rhodes University, Grahamstown, 6140, S. Afr.

SOURCE: Journal of Molecular Catalysis A: Chemical (2001), 176(1-2), 29-40  
 CODEN: JMCCF2; ISSN: 1381-1169

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The relative efficiencies for the oxidn. of trichlorophenol (TCP) and pentachlorophenol (PCP), sensitized by sulfonated **phthalocyanine** complexes contg. Zn, Al, Sn and Si as central metals, were studied in aq. solns. For the first time, sulfonated silicon and tin **phthalocyanines** were synthesized and their activity towards photosensitization of singlet oxygen and photo-oxidn. of polychlorophenols was examd. The efficiency of the sensitized photo-oxidative degrdn. of polychlorophenols depends not only on singlet oxygen quantum yield of sensitizer, but also on its stability. The influence of substrate structure and the pH of the soln. on the photo-oxidn. efficiency, as well as on the sensitizer photodegrdn. were studied. It was found that the contribution of the Type II (singlet oxygen-mediated) mechanism to the relative efficiency of the photosensitized photo-oxidn. of the phenol, decreased from phenol to p-chlorophenol, TCP and PCP, whereas Type I radical pathway increased. The results obtained for PCP give evidence that electron transfer from the excited sensitizer to the substrate in its unionized form is responsible for enhanced sensitizer photodegrdn.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:673224 HCAPLUS

DOCUMENT NUMBER: 136:2294

TITLE: Tryptophan-dependent sensitized photoinactivation of colicin E1 channels in bilayer lipid membranes

AUTHOR(S): Rokitskaya, T. I.; Zakharov, S. D.; Antonenko, Y. N.; Kotova, E. A.; Cramer, W. A.

CORPORATE SOURCE: Moscow State University, A.N. Belozersky Institute of Physico-Chemical Biology, Moscow, 119899, Russia

SOURCE: FEBS Letters (2001), 505(1), 147-150  
 CODEN: FEBLAL; ISSN: 0014-5793

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The bacterial toxin colicin E1 is known to induce voltage-gated currents across a planar bilayer lipid membrane. In the present study, it is shown that the colicin-induced current decreased substantially upon illumination of the membrane in the presence of the photosensitizer, aluminum **phthalocyanine**. This effect was almost completely abolished by the **singlet oxygen** quencher, sodium azide. Using single tryptophan mutants of colicin E1, Trp495 was identified as the amino acid residue responsible for the sensitized photodamage of the

colicin channel activity. Thus, the distinct participation of a specific amino acid residue in the sensitized photoinactivation of a defined protein function was demonstrated. It is suggested that Trp495 is critical for the translocation and/or anchoring of the colicin channel domain in the membrane.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:140644 HCAPLUS

DOCUMENT NUMBER: 134:302913

TITLE: Photokinetics in **tetraphenylporphyrin** - molecular oxygen system at gas/solid interfaces: effect of singlet oxygen quenchers on oxygen-induced delayed fluorescence

AUTHOR(S): Levin, Peter P.; Costa, Silvia M. B.

CORPORATE SOURCE: Centro de Quimica Estrutural, Instituto Superior Tecnico, Lisbon, 1049-001, Port.

SOURCE: Chemical Physics (2001), 263(2-3), 423-436

CODEN: CMPHC2; ISSN: 0301-0104

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The oxygen quenching of excited states and concomitant delayed fluorescence (DF) of meso-**tetraphenylporphyrin** (TPP) adsorbed on alumina (Al<sub>2</sub>O<sub>3</sub>) were studied at different TPP and O<sub>2</sub> concns. and temps. by the diffuse-reflectance laser flash technique. The formation of 102 in the course of 3TPP quenching by 302 is followed by the energy transfer from 102 to 3TPP (102 feedback) with the generation of TPP fluorescent state. The global kinetic anal. of DF revealed variations on kinetic parameters with surface loading which match the aggregation of TPP on the surface. In concd. samples the energy exchange between 102 and 302 accelerates the 102 feedback more than 10 times. The key role of 102 in oxygen-induced DF is confirmed by the DF quenching by coadsorbed 102 quenchers (NaN<sub>3</sub>, 3-methylindole, 1,4-diazabicyclo[2.2.2]octane). This process is in part controlled by the surface which enhances the efficiencies of amine quenchers but reduces that of NaN<sub>3</sub> when compared with the corresponding efficiencies in soln.

REFERENCE COUNT: 61 THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:803575 HCAPLUS

DOCUMENT NUMBER: 134:123452

TITLE: Photocatalytic decomposition of trichlorophenol by zinc(II) **phthalocyanine** derivatives in aerated organic solvents

AUTHOR(S): Kasuga, K.; Fujita, A.; Miyazako, T.; Handa, M.; Sugimori, T.

CORPORATE SOURCE: Department of Material Science, Faculty of Science and Engineering, Shimane University, Matsue, 690-8504, Japan

SOURCE: Inorganic Chemistry Communications (2000), 3(11), 634-636

CODEN: ICCOFP; ISSN: 1387-7003

PUBLISHER: Elsevier Science S.A.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Trichlorophenol was photodecomposed by irradiation with visible light using zinc(II) **phthalocyanine** derivs. as photosensitizers in aerated

org. solvents. An oxidative quenching pathway via a generation of hyperoxide was proposed.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:469936 HCAPLUS

DOCUMENT NUMBER: 133:234504

TITLE: Inhibition of **phthalocyanine**-sensitized photohemolysis of human erythrocytes by polyphenolic antioxidants: description of quantitative structure-activity relationships

AUTHOR(S): Maroziene, A.; Kliukiene, R.; Sarlauskas, J.; Cenas, N.

CORPORATE SOURCE: Institute of Biochemistry, Vilnius, Lithuania

SOURCE: Cancer Letters (Shannon, Ireland) (2000), 157(1), 39-44

CODEN: CALEDQ; ISSN: 0304-3835

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Polyphenolic antioxidants protected against Al-**phthalocyanine** tetrasulfonate-sensitized photohemolysis of human erythrocytes. A quant. structure-activity relationship has been obtained to describe the protective effects of di- and trihydroxybenzenes:  $\log cI50$  ( $\mu M$ ) =  $(1.8620 \pm 0.15565) + (3.6366 \pm 0.28245) E17$  (V) -  $(0.4034 \pm 0.0765) \log P$  ( $r^2 = 0.8367$ ), where  $cI50$  represents the concns. of compds. for the 2-fold increase in the lag-phase of hemolysis,  $E17$  represents the compd. single-electron oxidn. potential, and  $P$  represents the octanol/water partition coeff. The  $cI50$  for quercetin and taxifolin were close, and  $cI50$  for morin, kaempferol and hesperetin were lower than might be predicted by this equation. The protection from hemolysis by **azide**, a quencher of **singlet oxygen** (102) was accompanied by increase in  $cI50$  of polyphenols, indicating that azide and polyphenols competed for the same damaging species, 102. These findings point out to two factors, detg. the protective efficiency of polyphenols against 102, namely, ease of electron donation and lipophilicity.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:442009 HCAPLUS

DOCUMENT NUMBER: 133:64103

TITLE: High energy phototherapeutic agents

INVENTOR(S): Dees, H. Craig; Scott, Timothy; Smolik, John; Wachter, Eric

PATENT ASSIGNEE(S): Photogen, Inc., USA

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037927	A1	20000629	WO 1999-US30156	19991216
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,				

MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,  
 SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,  
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,  
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 CA 2252782 AA 19980507 CA 1997-2252782 19971027  
 EP 1032321 A1 20000906 EP 1997-948121 19971027  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI  
 JP 2001503748 T2 20010321 JP 1998-520604 19971027  
 CA 2252783 AA 19980507 CA 1997-2252783 19971028  
 EP 977592 A1 20000209 EP 1997-946336 19971028  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI  
 JP 2000511929 T2 20000912 JP 1998-520696 19971028  
 US 5998597 A 19991207 US 1997-989231 19971211  
 US 6331286 B1 20011218 US 1998-216787 19981221  
 BR 9916398 A 20010911 BR 1999-16398 19991216  
 EP 1192450 A1 20020403 EP 1999-967402 19991216  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO  
 US 2002033989 A1 20020321 US 2001-779808 20010208  
 PRIORITY APPLN. INFO.: US 1998-216787 A 19981221  
 US 1996-739801 A 19961030  
 US 1996-741370 A 19961030  
 WO 1997-US19249 W 19971027  
 WO 1997-US19527 W 19971028  
 WO 1999-US30156 W 19991216  
 US 2000-187958P P 20000309  
 AB A high energy phototherapeutic agent or radiosensitizer comprises a  
 halogenated xanthene, or an agent that exhibits a preference for concn. in  
 biol. sensitive structures in diseased tissues. Some examples of the  
 halogenated xanthenes such as dibromo- or **diiodofluorescein** and  
 their properties are given.  
 REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT  
 L78 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:54727 HCAPLUS  
 DOCUMENT NUMBER: 132:292115  
 TITLE: Reactive oxygen species in essential hypertension and  
 non-insulin-dependent diabetes mellitus  
 AUTHOR(S): Orie, Nelson N.; Zidek, Walter; Tepel, Martin  
 CORPORATE SOURCE: Universitätsklinik Marienhospital, University of  
 Bochum, Bochum, Germany  
 SOURCE: American Journal of Hypertension (1999), 12(12, Pt. 1  
 & 2), 1169-1174  
 CODEN: AJHYE6; ISSN: 0895-7061  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB To evaluate whether increased levels of reactive oxygen species (ROS) are  
 involved in the pathogenesis of essential hypertension (EH) and  
 non-insulin-dependent diabetes mellitus (NIDDM), both resting and  
 stimulated levels of intracellular ROS were measured in lymphocytes from  
 patients with EH (n = 10), NIDDM (n = 16) and age-matched healthy  
 individuals (control subjects, n = 19). ROS was monitored with the dye,  
**dihydrorhodamine-123** (DHR; 1 .mu.mol/L) in the presence or absence  
 of superoxide dismutase (superoxide scavenger), sodium **azide** (

singlet oxygen/hydrogen peroxide scavenger), genistein (tyrosine kinase inhibitor), or bisindolylmaleimide (protein kinase C inhibitor). Simultaneous monitoring of cytosolic  $[Ca^{2+}]_i$  was done with fura-2. Resting ROS levels were significantly higher in NIDDM (4.71  $\pm$  0.25 nmol/106 cells; mean  $\pm$  SEM,  $P < .05$ ) compared with EH (4.03  $\pm$  0.22 nmol/106 cells) or controls (4.05  $\pm$  0.15 nmol/106 cells). The formyl-Met-Leu-Phenylalanine-(fMLP)-induced ROS generation was significantly higher in NIDDM (21.92  $\pm$  2.23 nmol/106 cells;  $P < .05$ ) compared with EH (14.58  $\pm$  1.90 nmol/106 cells) or control (16.06  $\pm$  1.22 nmol/106 cells). The fMLP-induced ROS increase was significantly reduced in the presence of sodium azide in all groups ( $P < .01$ ) but was largely unaffected in the presence of SOD. Genistein and bisindolylmaleimide significantly inhibited the fMLP-induced ROS in all groups. The fMLP-induced  $[Ca^{2+}]_i$  increase was significantly higher in NIDDM (71  $\pm$  12 nmol/L,  $P < .01$ ) compared with EH (42  $\pm$  4 nmol/L) and control subjects (35  $\pm$  3 nmol/L). Phytohemagglutinin was more effective in increasing  $[Ca^{2+}]_i$  than ROS. It is concluded that ROS may play a role in the metabolic syndrome of NIDDM but not in EH.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:645815 HCAPLUS

DOCUMENT NUMBER: 131:282668

TITLE: Oxidative stress in photodynamic herbicidal action of 5-aminolevulinic acid

AUTHOR(S): Tripathy, B. C.; Singhal, G. S.

CORPORATE SOURCE: School of Life Sciences, Jawaharlal Nehru University, New Delhi, 110067, India

SOURCE: Concepts in Photobiology (1999), 668-688. Editor(s): Singhal, G. S. Narosa: New Delhi, India. CODEN: 68GDZ4

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Tetrapyrrole biosynthesis can be manipulated to induce the accumulation of photodynamic **porphyrins** for herbicidal action. Chems. used as photodynamic herbicides are, 5-aminolevulinic acid (ALA), the **porphyrin** precursor; di-Ph ether and allied compds., **protoporphyrinogen** oxidase inhibitors; and modulators of the heme and chlorophyll biosynthetic pathways such as 2,2'-bipyridyl and 1,10 phenanthroline. Protox inhibitors cause max. accumulation of **protoporphyrin IX** whereas ALA-based photodynamic herbicides induce overaccumulation of Mg-tetrapyrroles. Cucumber plants were sprayed with 20 mM soln. of ALA, the precursor of tetrapyrroles, and then incubated in darkness for 14 h. Upon transfer to light (2000  $\mu$ mol  $m^{-2} s^{-1}$ ), the plants died after 6 h of exposure due to photodynamic damage and their Photosystem II (PS II) and Photosystem I (PS I) photochem. reactions were impaired. Thylakoid membranes prep. in darkness from control and 2 mM ALA-treated plants were illuminated (250  $\mu$ mol  $m^{-2} s^{-1}$ ) in the presence of scavengers of active oxygen species. The **singlet oxygen** scavengers histidine and sodium **azide** protected the thylakoid membrane linked function of PS II from photodynamic damage. However, the hydroxyl radical scavenger formate and the superoxide radical scavengers superoxide dismutase and 1, 2-dihydroxybenzene-3, 5-disulfonic acid failed to protect the PS II reaction. Non-phototransformable protochlorophyllide was the most abundant pigment in the thylakoid membranes isolated from ALA-treated plants and acted as a type II photosensitizer. Superoxides produced by the control and treated thylakoid membranes in light were abolished by diuron suggesting that type I photosensitization reaction due to protochlorophyllide is nearly absent

in ALA-treated plants. However, superoxide produced by the photosynthetic electron transport chain need to be dissipated by detoxifying enzymes, superoxide dismutase, ascorbate peroxidase and glutathione reductase. Due to photodynamic reactions superoxide dismutase activity was not affected whereas the ascorbate peroxidase and glutathione reductase activities were impaired suggesting that besides singlet oxygen which is the primary and immediate cause of photodynamic damage, impairment of two enzymes responsible for detoxification of superoxide generated by univalent redn. of oxygen by the photosynthetic electron transport chain would substantially contribute to the death of the plant. Because of its environmental safety, ALA and allied compds. have the potential of becoming important com. herbicides.

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:787059 HCAPLUS

DOCUMENT NUMBER: 128:111943

TITLE: Metal sites in small blue copper proteins, blue copper oxidases and vanadium-containing enzymes

AUTHOR(S): Messerschmidt, Albrecht

CORPORATE SOURCE: Max-Planck-Inst. Biochemie, Martinsried, D-82152, Germany

SOURCE: Struct. Bonding (Berlin) (1998), 90 (Metal Sites in Proteins and Models: Redox Centres), 37-68  
CODEN: STBGAG; ISSN: 0081-5993

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review, with 113 refs. The coordination geometries of metal sites in cupredoxins, mutants and metal derivs. of cupredoxins, multi-copper oxidases and a vanadium-contg. chloroperoxidase as derived from x-ray crystallog. are described. Correlations with their spectroscopic, electrochem., electron transfer and catalytic properties are discussed. X-ray crystallog., EPR and Resonance Raman spectroscopy of copper sites in cupredoxins and mutants have led to a classification ranging from type 1 trigonal, type 1 distorted tetrahedral, type 1.5 to type 2. The mutation of copper ligands in azurin or amino acids close to the copper site changes the redox potential in a range of  $\pm 0.140$  mV, only. The high redox potential of **rusticyanin** of 680 mV (azurin, 380 mV) should be mainly due to the special protein environment of the copper site (high proportion of hydrophobic residues). The type 1 and trinuclear copper centers of the multi-copper oxidases ascorbate oxidase, laccase and ceruloplasmin are presented. The metal sites of **type 2** depleted, fully-reduced peroxide and **azide** forms of ascorbate oxidase, as detd. by x-ray crystallog., are discussed in terms of the mechanistic properties of these enzymes. The first x-ray structure of a vanadium-contg. protein, namely of a chloroperoxidase from the fungus *Curvularia inaequalis*, is briefly discussed. The protein fold is mainly  $\alpha$ -helical with two four-helix bundles. In the x-ray structure, which is an azide:enzyme complex, the vanadium exhibits a simple unexpected coordination geometry, namely, a trigonal bipyramidal coordination with three non-protein oxygen ligands (VO<sub>3</sub> group), one nitrogen ligand from a histidine and one nitrogen from the exogenous azide ligand.

L78 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:341094 HCAPLUS

DOCUMENT NUMBER: 127:14906

TITLE: Effects of UV-sensitization of **hematoporphyrin**



on lipid hydroperoxides in erythrocytes and on their hemolysis

AUTHOR(S): Uchino, Tadashi; Tokunaga, Hiroshi; Kijima, Keiji; Ando, Masanori

CORPORATE SOURCE: Div. Environ. Chem., Natl. Inst. Health Sci., Tokyo, 158, Japan

SOURCE: Jpn. J. Toxicol. Environ. Health (1997), 43(2), 101-107

CODEN: JJTHEC; ISSN: 0013-273X

PUBLISHER: Pharmaceutical Society of Japan

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We have already reported the effect of UV-A (UVA)-sensitization of **hematoporphyrin** (HP) on the prodn. of lipid hydroperoxides in erythrocytes and on their hemolysis. In this report, we investigated these effects under UV-B (UVB) irradiation and compared the results with those under UVA irradiation. It was found that an increase in lipid hydroperoxide preceded hemolysis, and that the UVB irradiation resulted in an increase in phosphatidylethanolamine hydroperoxide (PEOOH) and 2-thiobarbituric acid reactive substances (TBA-RS) at an earlier stage in comparison with UVA irradiation. Under either UVA or UVB irradiation, hemolysis was inhibited by anti-oxidants such as sodium **azide** and ascorbic acid ( **singlet oxygen** scavengers), but not by mannitol, sorbitol (hydroxyl radical scavengers) or superoxide dismutase (SOD) (superoxide radical scavenger). These results suggest that singlet oxygen (1O<sub>2</sub>) produced by UV irradiation peroxidized the lipids of erythrocyte membranes, and therefore, the hemolysis of erythrocytes occurred when the amt. of hydroperoxides increased to a const. level, but auto-oxidation of lipids did not affect the hemolysis.

L78 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:587405 HCAPLUS

DOCUMENT NUMBER: 125:241938

TITLE: Photosensitization of **uroporphyrin** augments the ultraviolet A-induced synthesis of matrix metalloproteinases in human dermal fibroblasts

AUTHOR(S): Herrmann, Gernot; Wlaschek, Meinhard; Bolsen, Klaus; Prenzel, Klaus; Goerz, Guenter; Scharffetter-Kochanek, Karin

CORPORATE SOURCE: Department Dermatology, Heinrich-Heine-University Dusseldorf, Germany

SOURCE: J. Invest. Dermatol. (1996), 107(3), 398-403

CODEN: JIDEAE; ISSN: 0022-202X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Porphyrin cutanea tarda is characterized by severe connective tissue damage in sun-exposed skin. The regulated synthesis and degradation of the extracellular matrix by various matrix metalloproteinases (MMPs) depends on its amount and composition within the skin. In this study, we therefore asked whether long-wave UV irradiation (340-450 nm) in conjunction with **uroporphyrin** I could modulate the synthesis of MMPs with substrate specificities for dermal (collagens I, III, V; proteoglycans) and basement membrane components (collagens IV, VII; fibronectin; laminin) and whether synthesis of the counteracting tissue inhibitor of metalloproteinases is also affected. After irradiation of **uroporphyrin**-pretreated fibroblasts, specific mRNAs of MMP-1 and MMP-3 increased concomitantly up to 2.7-fold compared with UV-irradiated cells and up to 10-fold compared with mock-irradiated or **uroporphyrin** I-treated controls. In contrast, mRNA levels of tissue inhibitor of metalloproteinases remained unaltered. Similar results were obtained by immunoprecipitation. Gelatin and

casein zymog. revealed increased proteolytic activity of MMP-2 and MMP-3 in blister fluids of patients with porphyria cutanea tarda, indicating that similar events may occur in vivo. Using deuterium oxide as enhancer and sodium azide as quencher of singlet oxygen, we could increase or reduce MMP synthesis, suggesting that singlet oxygen is the major intermediate in the up-regulation of MMPs after irradiation of uroporphyrin-pretreated fibroblasts. Taken together, our results show that UV irradiation alone, and to a greater extent in conjunction with uroporphyrin I, results in an unbalanced synthesis of MMPs that may contribute to the destruction of the dermis and basement membrane, leading to blistering and accelerated photoaging in porphyria cutanea tarda patients.

L78 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:317564 HCAPLUS

DOCUMENT NUMBER: 125:4587

TITLE: Effect of lipophilic antioxidants of peroxidation of liposome membranes photosensitized by hematoporphyrin derivatives upon He-Ne laser irradiation

AUTHOR(S): Klebanov, G. I.; Teselkin, Yu. O.; Babenkova, I. V.; Zhambalova, B. A.; Vandanmagsar, B.; Nesterova, O. A.; Stranadko, E. F.

CORPORATE SOURCE: Russian State Medical University, Moscow, Russia

SOURCE: Biol. Membr. (1996), 13(2), 133-137

CODEN: BIMEE9; ISSN: 0233-4755

DOCUMENT TYPE: Journal

LANGUAGE: Russian

AB Lipid peroxidation (LPO) of liposomes photosensitized by hematoporphyrin derivs. (HPD) induced by low-intensity He-Ne laser irradiation (632.8 nm) was studied. The LPO was estimated from the malondialdehyde (MDA) formation in the thiobarbituric acid assay. Laser irradiation increased the levels of MDA in a dose-dependent manner (5-30 J/cm<sup>2</sup>). The LPO of liposomes did not develop in the absence of HPD. Natural lipophilic antioxidants, such as  $\alpha$ -tocopherol, lycopene, and dihydroquercetin, inhibited the LPO of liposome membranes more efficiently than a singlet-oxygen quencher sodium azide at an irradiation dose of 10.5 J/cm<sup>2</sup>. It may be assumed that singlet oxygen generated in the membrane lipid phase is responsible for the LPO photosensitization by HPD in liposomes upon laser irradiation.

L78 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:26271 HCAPLUS

DOCUMENT NUMBER: 124:83130

TITLE: Kinetics of plasma membrane and mitochondrial alterations in cells undergoing apoptosis

AUTHOR(S): Lizard, Gerard; Fournel, Sylvie; Genestier, Laurent; Dhedin, Nathalie; Chaput, Christophe; Flacher, Monique; Mutin, Mireille; Panaye, Genevieve; Revillard, Jean-Pierre

CORPORATE SOURCE: Centre Commun de Cytometrie en Flux, Hopital Edouard Herriot, Lyon, Fr.

SOURCE: Cytometry (1995), Volume Date 1995, 21(3), 275-83

CODEN: CYTODQ; ISSN: 0196-4763

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Programmed cell death or apoptosis is characterized by typical morphological alterations. By transmission electron microscopy, apoptotic cells are identified by condensation of the chromatin in tight apposition to the nuclear envelope, alteration of the nuclear envelope and fragmentation of

the nucleus, whereas integrity of the plasma membrane and organelles is preserved. Conversely cells undergoing necrosis display an early disintegration of cytoplasmic membrane and swelling of mitochondria. In this study we assessed by flow cytometry the sequential alterations of forward angle light scatter, 90.degree. light scatter, and fluorescence assocd. with **fluorescein** diacetate, **rhodamine** 123, and propidium iodide in two human B cell lines undergoing apoptosis induced by the topoisomerase II inhibitor VP-16. The kinetics of these modifications were compared to those of cells undergoing **necrosis** induced by sodium **azide**. At the same time intervals, cells were examd. by transmission electron microscopy and by UV microscopy after staining with Hoechst 33342. The data show that sequential changes in light scatters and **fluorescein** diacetate are similar in cells undergoing apoptosis or necrosis, whereas apoptosis is characterized by a slightly delayed decrease of mitochondrial activity as assessed by **rhodamine** 123 staining. Surprisingly a part of cells undergoing apoptosis displayed an early uptake of propidium iodide followed by a condensation and then a fragmentation of their nuclei. It is concluded that uptake of propidium iodide is a very early marker of cell death which does not discriminate between necrosis and apoptosis. Along with biochem. criteria, nuclear morphol. revealed by staining with Hoechst 33342 would seem to be of the most simple and most discriminative assay of apoptosis.

L78 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:976511 HCAPLUS

DOCUMENT NUMBER: 124:159979

TITLE: A comparison of the photoproperties of zinc **phthalocyanine** and zinc

**naphthalocyanine** tetrasulfonates: model

sensitizers for the photodynamic therapy of tumors

AUTHOR(S): Spikes, John D.; van Lier, Johan E.; Bommer, Jerry C.

CORPORATE SOURCE: Department of Biology, University of Utah, Salt Lake City, UT, 84112, USA

SOURCE: J. Photochem. Photobiol., A (1995), 91(3), 193-8

CODEN: JPPCEJ; ISSN: 1010-6030

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Phthalo- and **naphthalocyanines** are of interest as sensitizers for the photodynamic therapy of tumors because of their strong absorption in the 680 and 760 nm ranges resp. Both zinc **phthalocyanine** and **naphthalocyanine** tetrasulfonates (ZnPcS4 and ZnNcS4) were aggregated and photochem. inactive in aq. buffer of pH 7.4, while in 10 mM cetyl pyridinium chloride in buffer they were monomeric and active. Therefore all these studies were carried out using the buffered detergent. The triplet lifetimes of ZnPcS4 and ZnNcS4 under argon were 490 and 110 .mu.s resp., with oxygen bimol. quenching consts. of 4.2.times.10<sup>9</sup> and 2.0.times.10<sup>8</sup> M<sup>-1</sup>s<sup>-1</sup> resp. Triplet decay curves in argon, air and 100% oxygen were first order, suggesting that there was little back reaction of the triplet states with oxygen as has been obsd. with some **naphthalocyanines**. The quantum yield of singlet oxygen generation by ZnPcS4 was 0.70 and that for ZnNcS4 was 0.25. Both compds. sensitized the photooxidn. of furfuryl alc., cysteine, histidine, methionine, tryptophan, tyrosine and guanosine; ZnPcS4 was three times more efficient than ZnNcS4. These reactions were 50% inhibited by about 0.5 mM **azide**, suggesting the involvement of **singlet oxygen**. Both sensitizers photobleached on illumination, with quantum yields of 1.7.times.10<sup>-5</sup> for ZnPcS4 and 4.2.times.10<sup>-3</sup> for ZnNcS4.

L78 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:660131 HCAPLUS

DOCUMENT NUMBER: 123:137536  
 TITLE: The effect of **porphyrin** and radiation on ferrochelatase and 5-aminolevulinic acid synthase in epidermal cells  
 AUTHOR(S): He, D.; Behar, S.; Nomura, N.; Sassa, S.; Taketani, S.; Lim, H. W.  
 CORPORATE SOURCE: Dermatology Service, Department of Veterans Affairs Medical Center, New York, NY, 10010, USA  
 SOURCE: Photodermatol., Photoimmunol. Photomed. (1995), 11(1), 25-30  
 CODEN: PPPHEW; ISSN: 0905-4383  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The effects of UV A (UVA) and blue light on ferrochelatase protein, and its mRNA level, in 5-aminolevulinic acid (ALA)-loaded A431 cells was evaluated. Western blot anal. of ferrochelatase protein showed a protein band of 43 kDa. There was a decrease in the protein concn. 24 h and 48 h after irradiation of these cells. In contrast, as judged by Northern blot anal., there was no change in ferrochelatase mRNA level. Measurement of ALA synthase activity showed an ALA dose-dependent but radiation-independent decrease of enzyme activity, suggesting an end-product feedback inhibition. Since reactive oxygen species generated by **porphyrin**-induced photochem. reaction may be involved in the decrease in ferrochelatase protein, the effect of scavengers of reactive oxygen species was evaluated by measuring **porphyrin** accumulation in irradiated, ALA-loaded A431 cells. **Porphyrin** accumulation was significantly decreased in the presence of **singlet oxygen** scavenger sodium **azide** (0.05 mM, 40.6% suppression) or hydroxyl radical scavenger mannitol (5.0 mM, 45.0% suppression). These data suggest that the photochem. reaction induced by **porphyrin** and irradiation resulted in a decrease in ferrochelatase protein content, but had no effect on ferrochelatase mRNA level nor on ALA synthase activity. The decrease in protein was partly mediated by the reactive oxygen species.

L78 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:270218 HCAPLUS  
 DOCUMENT NUMBER: 122:50083  
 TITLE: A simple in vitro method to detect singlet oxygen and to compare photodynamic activity using alkaline phosphatase  
 AUTHOR(S): Yadav, H. S.; Jain, V.  
 CORPORATE SOURCE: Dep. Biocybernetics, Inst. Nuclear Medicine Allied Sci., Delhi, 110 054, India  
 SOURCE: Indian J. Biochem. Biophys. (1994), 31(6), 490-5  
 CODEN: IJBBBQ; ISSN: 0301-1208  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB A simple, sensitive and reliable in vitro method based on photodynamic inactivation of alk. phosphatase to detect singlet oxygen and for evaluating relative photosensitizing efficiencies of photosensitizers such as **hematoporphyrin** (Hp) and **phthalocyanines** has been developed and compared with photobleaching of p-nitroso di-Me aniline (RNO) and photooxidation of L-tryptophan. Inactivation of alk. phosphatase is dependent both on light fluence and sensitizer concn. Scavengers like mannitol and **azide** anion indicated the involvement of **singlet oxygen** in the deactivation of alk. phosphatase, since **azide** anion provided concn. dependent protection whereas mannitol had no effect and that compared to ordinary water, photoinactivation of alk. phosphatase was three times higher in 65% D2O. Alk. phosphatase

appears to be resistant to free radical attack (particularly to OH radicals) since hydrogen peroxide alone or in presence of ferrous ions did not reduce the enzyme activity and mannitol or azide anion gave no significant protection when alk. phosphatase was irradiated with Co-60 gamma rays up to 2 KGy. With the present method using red light, the chloroaluminum **phthalocyanine** sulfonates prepd. by sulfonation showed higher and the corresponding condensation product lower photodynamic activity; Hp being intermediate and Mn- and Gd-**phthalocyanines** had no photodynamic activity.

L78 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:26538 HCAPLUS

DOCUMENT NUMBER: 120:26538

TITLE: Photobleaching of mono-L-aspartyl chlorin e6 (NPe6): a candidate sensitizer for the photodynamic therapy of tumors

AUTHOR(S): Spikes, John D.; Bommer, Jerry C.

CORPORATE SOURCE: Dep. Biol., Univ. Utah, Salt Lake City, UT, 84112, USA

SOURCE: Photochem. Photobiol. (1993), 58(3), 346-50

CODEN: PHCBAP; ISSN: 0031-8655

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Most sensitizers used for the photodynamic therapy (PDT) of tumors photobleach upon illumination. Thus, it is of interest to examine the photobleaching behavior of new sensitizers proposed for use in PDT. This report surveys the quantum yields and kinetics of the photobleaching of mono-L-aspartyl chlorin e6 (NPe6), a hydrophilic chlorin that has many of the photoproperties desirable in a sensitizer for clin. PDT. It is a very effective sensitizer for the PDT of several types of model tumors in animals and is now in Phase I clin. trials. The quantum yield of NPe6 photobleaching in pH 7.4 phosphate buffer in air was 8.2 .times. 10<sup>-4</sup>; this is greater than the yields for typical **porphyrin** photosensitizers. For example, the yields for **hematoporphyrin** and **uroporphyrin** are 4.7 .times. 10<sup>-5</sup> and 2.8 .times. 10<sup>-5</sup>, resp. The yield decreases significantly in org. solvents of low dielec. const. The Sn deriv. of NPe6 was more light stable than NPe6 (yield = 5.7 .times. 10<sup>-6</sup>), while the Zn deriv. was more sensitive (yield = 1.9 .times. 10<sup>-2</sup>). Oxygen appeared to be necessary for the photobleaching of NPe6; however, bleaching was not inhibited by 100 mM **azide**, an efficient quencher of **singlet oxygen**. The photooxidizable substrates cysteine, dithiothreitol and furfuryl alc. increased the quantum yield of photobleaching 2-4-fold, while the electron acceptor, metronidazole, increased it almost 6-fold. Photobleaching yields for several other chlorins were also measured.

L78 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:2468 HCAPLUS

DOCUMENT NUMBER: 120:2468

TITLE: Evidence for singlet oxygen-induced cross-links and aggregation of collagen

AUTHOR(S): Kakehashi, Akihiro; Akiba, Jun; Ueno, Norio;

Chakrabarti, Bireswar

CORPORATE SOURCE: Schepens Eye Res. Inst., Harvard Med. Sch., Boston, MA, 02114, USA

SOURCE: Biochem. Biophys. Res. Commun. (1993), 196(3), 1440-6

CODEN: BBRC9; ISSN: 0006-291X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Singlet oxygen, generated by **hematoporphyrin**-photosensitized reaction, caused insolubilization and an increase in mol. wt. of acid sol.

type I collagen and vitreous collagen as manifested in sodium dodecyl sulfate polyacrylamide gel electrophoresis. No such changes in the mol. properties of collagen could be obsd. when the irradiation was carried out in the presence of sodium azide, a singlet oxygen quencher. The increase in mol. wt. and insolubilization of the collagen soln. was attributed to extensive cross-links in the protein mols.

L78 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:448821 HCAPLUS

DOCUMENT NUMBER: 119:48821

TITLE: Formation of 2,5-dihydroxybenzoic acid during the reaction between singlet oxygen ( $^1O_2$ ) and salicylic acid: analysis by ESR oximetry and HPLC with electrochemical detection

AUTHOR(S): Kalyanaraman, B.; Ramanujam, Sujatha; Singh, Ravinder J.; Joseph, Joy; Feix, Jimmy B.

CORPORATE SOURCE: Biophys. Res. Inst., Med. Coll. Wisconsin, Milwaukee, WI, 53226, USA

SOURCE: J. Am. Chem. Soc. (1993), 115(10), 4007-12

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The oxygen consumption vis-a-vis  $^1O_2$  prodn. during irradiation of dyes such as rose bengal, **merocyanine-540**, and aluminum **phthalocyaninetetrasulfonate** in the presence of salicylic acid was measured by ESR oximetry. Concomitantly, formation of 2,5-dihydroxybenzoic acid (2,5-DHBA) in the same sample was analyzed by HPLC-EC. Both  $O_2$  consumption and 2,5-DHBA formation were stimulated by  $D_2O$ , quenched by azide, unaffected in the presence of catalase, superoxide dismutase, and hydroxyl radical scavengers (ethanol, formate, etc.), and vastly diminished under  $N_2$ . The stoichiometry between  $^1O_2$  consumption and 2,5-DHBA formation was detd. to be ca. 0.5. On the basis of expts. using histidine, the chem. rate const. for the reaction between  $^1O_2$  and salicylic acid was detd. to be 0.20 times  $10^6 M^{-1} s^{-1}$ . Furthermore,  $^1O_2$  generated from the thermal decompn. of the water-sol. endoperoxide of 3,3'-(1,4-naphthylene)dipropionate (NDPO $_2$ ) was shown to react with salicylic acid to form 2,5-DHBA as the major product. Exclusive formation of 2,5-DHBA is highly diagnostic of  $^1O_2$  intermediacy in photochem. systems and in biochem. systems lacking metabolic activity. HPLC-EC is thus a valuable adjunct to ESR oximetry in the characterization of  $^1O_2$  and may, on the basis of the selectivity of this reaction, provide a sensitive anal. method for detecting  $^1O_2$  intermediacy.

L78 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:485980 HCAPLUS

DOCUMENT NUMBER: 117:85980

TITLE: Reactive oxygen species in the photosensitization of retinal pigment epithelial cells by rose bengal

AUTHOR(S): Menon, I. Aravind; Basu, Prasanta K.; Persad, Suruj D.; Das, Arpita; Wiltshire, J. Diane

CORPORATE SOURCE: Dep. Med., Univ. Toronto, Toronto, ON, Can.

SOURCE: J. Toxicol., Cutaneous Ocul. Toxicol. (1992), 11(4), 269-83

CODEN: JTOTDO; ISSN: 0731-3829

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rose bengal (RB) is a **fluorescein** deriv. used as a vital stain in certain ophthalmic diagnostic procedures. RB is a potent photosensitizer and has been used as a model for photosensitized reactions involving singlet oxygen. UV-visible (UV-VIS) irradiation of RB with

nitroblue tetrazolium (NBT) in the absence of glutathione (GSH) induced the redn. of NBT. However since superoxide dismutase (SOD) did not inhibit this NBT redn., it seems to be not mediated by superoxide but due to the direct redn. of NBT by the excited state of RB. UV-VIS irradiation of RB, NBT, and 1-5 mM GSH reduced larger amounts of NBT. Moreover, SOD partially inhibited the NBT redn. under these conditions, indicating the formation of superoxide. The optimal pH for the formation of superoxide was 7-9. Superoxide formation during UV-VIS irradiation of RB and GSH was not inhibited by the **singlet oxygen** scavengers

.beta.-carotene, sodium **azide**, or 1,4-diazabicyclo[2.2.2]octane (DABCO), indicating that the superoxide formation was not mediated by singlet oxygen. These findings show that superoxide was formed only during UV-VIS irradiation of RB and GSH; exposure of RB and GSH to visible light (VIS) did not produce any detectable amount of superoxide. When RB and 0.1 mM GSH were irradiated, significant amounts of H<sub>2</sub>O<sub>2</sub> could be detected. Since this was enhanced by the addition of SOD to the system, it may be concluded that it was mediated by superoxide. The lysis of RPE cells upon UV-VIS irradiation in the presence of RB was partially inhibited by catalase, indicating mediation by H<sub>2</sub>O<sub>2</sub>. This inhibitory effect of catalase was more pronounced in the presence of a low concentration of GSH. However, when VIS was used for the irradiation, catalase did not affect cell lysis. The results demonstrate one instance in which the mechanism of cytotoxicity induced by a particular photosensitizer varies depending upon the emission spectrum of the irradiation source and the components of the medium in which the cells or tissues are suspended.

L78 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:465583 HCAPLUS

DOCUMENT NUMBER: 117:65583

TITLE: Quantum yields and kinetics of the photobleaching of **hematoporphyrin**, Photofrin II, tetra(4-sulfonatophenyl)porphine and **uroporphyrin**

AUTHOR(S): Spikes, John D.

CORPORATE SOURCE: Dep. Biol., Univ. Utah, Salt Lake City, UT, 84112, USA

SOURCE: Photochem. Photobiol. (1992), 55(6), 797-808

CODEN: PHCBAP; ISSN: 0031-8655

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Porphyrins** used as sensitizers for the photodynamic therapy (PDT) of tumors are progressively destroyed (photobleached) during illumination. If the **porphyrin** bleaches too rapidly, tumor destruction will not be complete. However, with appropriate sensitizer doses and bleaching rates, irreversible photodynamic injury to the normal tissues surrounding the tumor, which retain less sensitizer, may be significantly decreased. This paper surveys the quantum yields and kinetics of the photobleaching of 4 **porphyrins**, i.e., **hematoporphyrin** (HP), Photofrin II (PF II), tetra(4-sulfonatophenyl)porphine (TSPP), and **uroporphyrin** I (URO). The initial quantum yields of photobleaching, as measured in pH 7.4 phosphate buffer in air, were  $4.7 \times 10^{-5}$ ,  $5.4 \times 10^{-5}$ ,  $9.8 \times 10^{-6}$ , and  $2.8 \times 10^{-5}$  for HP, PF II, TSPP, and URO, resp.; thus, the rates of photobleaching are rather slow. Low oxygen concentration (2  $\mu$ M) significantly reduced the photobleaching yields. However, D<sub>2</sub>O increased the yields only slightly, and the **singlet oxygen** quencher, **azide**, had no effect, even at 0.1M. Photosensitizing **porphyrins** in body fluids, cells, and tissues may be closely associated with various photooxidizable molecules and electron acceptors and donors. Therefore, selected model compounds in these categories were examined for their effects on **porphyrin** photobleaching. A no. inhibited and/or accelerated

photobleaching, depending on the compd., the **porphyrin**, and the reaction conditions. For example, 1.0 mM furfuryl alc. increased the photobleaching yields of HP and URO >5-fold, with little effect on PF II or TSPP. In contrast, the electron acceptor, Me viologen, increased the photobleaching yield of TSPP >10-fold, with little accelerating effect on the other **porphyrins**. These results suggest that the mechanism(s) of the photobleaching of **porphyrin** photosensitizers in cells and tissues during PDT may be complex.

L78 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:169042 HCAPLUS

DOCUMENT NUMBER: 116:169042

TITLE: Photodynamic effects of chloroaluminum **phthalocyanine** tetrasulfonate are mediated by singlet oxygen: in vivo and in vitro studies utilizing hepatic microsomes as a model membrane source

AUTHOR(S): Agarwal, Rajesh; Zaidi, Syed I. A.; Athar, Mohammad; Bickers, David R.; Mukhtar, Hasan

CORPORATE SOURCE: Skin Dis. Res. Cent., Univ. Hosp. Cleveland, Cleveland, OH, 44106, USA

SOURCE: Arch. Biochem. Biophys. (1992), 294(1), 30-7

CODEN: ABBIA4; ISSN: 0003-9861

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Chloroaluminum **phthalocyanine** tetrasulfonate (AlPcTS) is a promising photosensitizer for the photodynamic therapy (PDT) of cancer. In this study, the in vivo and in vitro photodestruction of hepatic microsomal membranes by AlPcTS was investigated and the role of reactive oxygen species in this process studied. Irradn. of hepatic microsomes prepd. from AlPcTS-pretreated SENCAR mice to .apprxeq.675 nm light resulted in rapid destruction of cytochrome P 450 and assocd. monooxygenase activities, and enhancement of lipid peroxidn. in a light-dose-dependent manner. The specificity of AlPcTS and light dependency on photodestruction of microsomal membranes was confirmed by Western blot anal. Similar results were obtained when AlPcTS was added in vitro to a suspension of hepatic microsomes prepd. from control animals followed by irradiation with .apprxeq.675 nm light. Among the quenchers of singlet oxygen, superoxide anion, hydrogen peroxide, and hydroxyl radical, only the quenchers of **singlet oxygen** such as sodium **azide**, histidine, and 2,5-dimethylfuran afforded substantial protection in a dose-dependent manner against AlPcTS-mediated photodestruction activities, and photoenhancement of lipid peroxidn. under both in vivo and in vitro conditions. These results suggest that lipid-rich microsomal membranes may be the potential targets of cell injury by AlPcTS-based PDT and that this process is mediated by singlet oxygen.

L78 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:148444 HCAPLUS

DOCUMENT NUMBER: 116:148444

TITLE: Involvement of singlet oxygen in 5-aminolevulinic acid-induced photodynamic damage of cucumber (Cucumis sativus L.) chloroplasts

AUTHOR(S): Chakraborty, Niranjana; Tripathy, Baishnab Charan  
CORPORATE SOURCE: Sch. Life Sci., Jawaharlal Nehru Univ., New Delhi, 110067, India

SOURCE: Plant Physiol. (1992), 98(1), 7-11

CODEN: PLPHAY; ISSN: 0032-0889

DOCUMENT TYPE: Journal



LANGUAGE: English

AB Cucumber (*Cucumis sativus*, cv Poinsette) plants were sprayed with 20 mM 5-aminolevulinic acid and then incubated in the dark for 14 h. The intact chloroplasts were isolated from the treated plants in the dark and were exposed to weak light (250  $\mu\text{mol}/\text{m}^2/\text{s}$ ). Within 30 min, photosystem II activity was reduced by 50%. The **singlet oxygen** (102) scavengers histidine and sodium **azide** ( $\text{NaN}_3$ ) significantly protected against the damage caused to photosystem II. The hydroxyl radical scavenger formate failed to protect the thylakoid membranes. The prodn. of 102 monitored as N,N-di-Me p-nitrosoaniline bleaching increased as a function of light exposure time of treated chloroplasts and was abolished by the 102 quencher  $\text{NaN}_3$ . Membrane lipid peroxidn., monitored as malondialdehyde prodn., was also significantly reduced when chloroplasts were illuminated in the presence of  $\text{NaN}_3$  and histidine. Protochlorophyllide was the most abundant pigment accumulated in intact chloroplasts isolated from 5-aminolevulinic acid-treated plants and was probably acting as type II photosensitizer.

L78 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:674474 HCAPLUS

DOCUMENT NUMBER: 115:274474

TITLE: Spectroscopic and chemical studies of the ascorbate oxidase trinuclear copper active site: comparison to laccase

AUTHOR(S): Cole, James L.; Avigliano, Luciana; Morpurgo, Laura; Solomon, Edward I.

CORPORATE SOURCE: Dep. Chem., Stanford Univ., Stanford, CA, 94305, USA

SOURCE: J. Am. Chem. Soc. (1991), 113(24), 9080-9

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The multicopper oxidases, laccase (I), ascorbate oxidase (II), and ceruloplasmin, contain type-1, -2, and -3 Cu sites. Detailed spectroscopic studies of azide binding to I previously demonstrated that the type-2 and the coupled binuclear type-3 centers form a trinuclear Cu cluster site that has been shown to be the active site in the multielectron redn. in  $\text{O}_2$ . A recent x-ray crystal structure of II indicated that this enzyme also contains a trinuclear site. In the present study, a combination of electronic spectroscopy and exogenous ligand perturbation was used to probe the geometric and electronic structures of the type-1 and the type-2-type-3 trinuclear sites in II. These results were compared to previous work on I. Low-temp. MCD spectra of the type-1 centers in II and **plastocyanin** were very similar, but the type-1 spectrum of I was different, indicating that the structure of the I blue-Cu center was perturbed. The contribution to the MCD spectrum by the type-2  $\text{Cu}^{2+}$  is identified by the effect of fluoride binding to the type-2 site, and the energies closely corresponded to the type-2 features in I. Azide equil. binding and kinetic measurements demonstrated that 3 different azide mols. coordinate to the trinuclear site. One azide bound as a bridging ligand between the type-2 site and the type-3 site in a manner that was similar to that previously obsd. in I. In contrast, the 2 other **azides** bound terminally to **type-2** and type-3 Cu sites, resp., whereas in I only a 2nd azide bound to the fully oxidized enzyme and bridged the type-2 and type-3 sites. This difference indicated the presence of a distortion of the II trinuclear site that prevented an addnl. **azide** from bridging the **type-2** and type-3 centers. The conservation of the type-2-type-3 bridged binding site for azide in the 2 enzymes suggested that this coordination mode is active in the irreversible 4-electron redn. of  $\text{O}_2$  to  $\text{H}_2\text{O}$  in the multicopper oxidases and

that only a single bridging coordination position is required for efficient 4-electron O<sub>2</sub> redn.

L78 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:256767 HCAPLUS

DOCUMENT NUMBER: 114:256767

TITLE: Photooxidation of Hypocrellin A - the influence of pH on the sensitized photooxidation of Hypocrellin A in aqueous solvents

AUTHOR(S): An, Jingyi; Jiang, Lijin; He, Jianjun

CORPORATE SOURCE: Inst. Photogr. Chem., Acad. Sin., Beijing, 100012, Peop. Rep. China

SOURCE: Chin. Sci. Bull. (1990), 35(22), 1933-4

CODEN: CSBUEF; ISSN: 1001-6538

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Photooxidn. of Hypocrellin A (HA) in aq. soln. was studied at pH 6-11.3. Quantum yield of HA photooxidn. was pH dependent. The marked changes of photooxidn. products and quantum yields in alk. solns. were related to their structural changes. There are 2 phenolic groups in the mol. of HA which exists as HA dianion form in alk. soln. The results suggest that the dianion form of HA is more susceptible to photooxidn. than HA mol. Results of quenching and sensitization expts. suggest that photooxidn. of HA in alk. soln. involves ground state HA and singlet oxygen (<sup>1</sup>O<sub>2</sub>).

L78 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:627057 HCAPLUS

DOCUMENT NUMBER: 113:227057

TITLE: Spectroscopic and chemical studies of the laccase trinuclear copper active site: geometric and electronic structure

AUTHOR(S): Cole, James L.; Clark, Patrick A.; Solomon, Edward I.

CORPORATE SOURCE: Dep. Chem., Stanford Univ., Stanford, CA, 94305, USA

SOURCE: J. Am. Chem. Soc. (1990), 112(26), 9534-48

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Laccase contains 4 Cu atoms: a type 1, a type 2, and a coupled binuclear type 3 center. The type 2 and type 3 centers comprise a trinuclear Cu cluster which is thought to represent the active site for the binding and multielectron redn. of O<sub>2</sub>. A combination of electronic spectroscopy, magnetic susceptibility, and exogenous ligand perturbation was used to probe the geometric and electronic structure of the trinuclear site. A type 1 Hg<sup>2+</sup>-substituted laccase deriv. was employed in order to remove the overlapping spectral contributions from the type 1 Cu<sup>2+</sup>. The ligand-field and charge-transfer transitions of the type 2 and type 3 Cu atoms were assigned by use of absorption, CD, and low-temp. MCD spectroscopies. The ligand-field transition energies indicated that all 3 Cu atoms had tetragonal geometries and that the 2 type 3 Cu atoms were unequiv. Magnetic susceptibility measurements defined the lower limit for the magnitude of the exchange interaction between the type 3 Cu atoms and probed type 2-type 3 interactions. The binding of the exogenous ligand, azide, to the trinuclear site produced characteristic azide f.w.darw. Cu<sup>2+</sup> charge-transfer features and also perturbed the type 2 and type 3 ligand-field transitions. Anal. of these spectral features demonstrated that azide bound as a bridging ligand between the type 2 site and 1 of the type 3 Cu atoms. In addn., a 2nd azide coordinated to the type 3 site with a lower binding const., and this second azide also strongly interacted with the type 2 site. The type 2-type 3 bridged binding of azide suggested that a

similar coordination mode is active in the irreversible binding and 4-electron redn. of O<sub>2</sub>. The 2nd azide binding provided a further demonstration of the differences between the laccase type 3 site and the coupled binuclear sites in **hemocyanin** and tyrosinase. A model for the magnetic interactions among the 3 Cu atoms in the resting and ligand-bound forms of the trinuclear site is presented.

L78 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1972:71726 HCAPLUS

DOCUMENT NUMBER: 76:71726

TITLE: Chemistry of **singlet oxygen**. XV.  
Irrelevance of **azide** trapping to mechanism  
of the ene reaction

AUTHOR(S): Foote, Christopher S.; Fujimoto, Ted T.; Chang, Yew C.

CORPORATE SOURCE: Dep. Chem., Univ. California, Los Angeles, Calif., USA

SOURCE: Tetrahedron Lett. (1972), (1), 45-8

CODEN: TELEAY

DOCUMENT TYPE: Journal

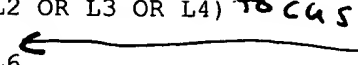
LANGUAGE: English

AB The addn. of singlet mol. O (1O<sub>2</sub>) in the presence of N<sub>3</sub>- to 2-methyl-2-pentene (I) occurred via a concerted ene reaction; an intermediate perepoxide was not involved in this reaction. The sensitized photooxidn. of I in aq. MeOH-NaN<sub>3</sub> gave a mixt. of allylic hydroperoxides and azido hydroperoxides. The ratio of these products was not related to the type of sensitizer; the amt. of allyl hydroperoxide was independent of the concn. of **Rhodamine B** (II) while the amt. of the azido peroxide increased with the concn. of II. The photo reaction of 1O<sub>2</sub> with I in MeOH contg. II, NaN<sub>3</sub>, and the O<sub>2</sub> acceptor dimethylfuran gave reduced yields of allylic hydroperoxides and approx. the same yield of the azido hydroperoxide indicating that both product types were formed in separate competing reactions. The kinetics of the sensitized photooxygenation in the presence of N<sub>3</sub>- supported this. The mechanism of these reactions was discussed.

# Inventn Search

CEPERLEY 09/898,885

=> d que l11

L1 345 SEA FILE=HCAPLUS ABB=ON PLU=ON RAJAGOPALAN R?/AU  
L2 49 SEA FILE=HCAPLUS ABB=ON PLU=ON BUGAJ J?/AU  
L3 48 SEA FILE=HCAPLUS ABB=ON PLU=ON DORSHOW R?/AU  
L4 44 SEA FILE=HCAPLUS ABB=ON PLU=ON ACHILEFU S?/AU  
L5 415 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4) *focus on*  
L6 93766 SEA FILE=HCAPLUS ABB=ON PLU=ON ?AZIDE?   
L7 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L5 AND L6  
L10 68 SEA FILE=REGISTRY ABB=ON PLU=ON (7429-91-6/BI OR 7439-89-6/BI  
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OR 7440-02-0/BI OR 7440-12-2/BI OR 7440-18-8/BI OR 7440-20-2/BI  
OR 7440-23-5/BI OR 7440-26-8/BI OR 7440-30-4/BI OR 7440-32-6/B  
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BI OR 7440-62-2/BI OR 79-08-3/BI OR 79-11-8/BI)  
L11 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L10 AND L7

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L11 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:204090 HCAPLUS

DOCUMENT NUMBER: 118:204090

TITLE: Complexes and compositions for magnetic resonance imaging and usage methods

INVENTOR(S): **Rajagopalan, Raghavan**; Wallace, Rebecca A.; Periasamy, Muthunadar P.

PATENT ASSIGNEE(S): Mallinckrodt Medical, Inc., USA

SOURCE: U.S., 8 pp.

CODEN: USXXAM

DOCUMENT TYPE: Patent

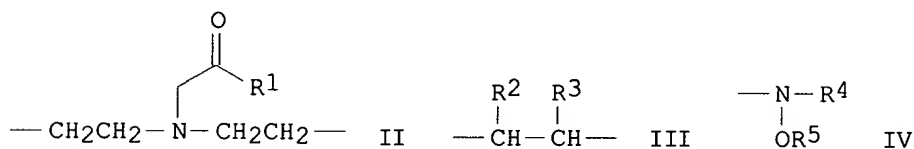
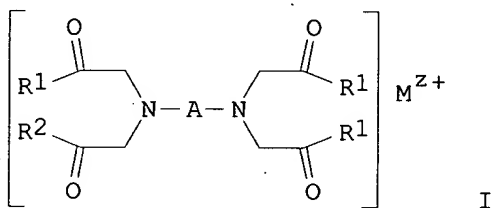
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5141740	A	19920825	US 1990-616450	19901121

OTHER SOURCE(S): MARPAT 118:204090  
GI



AB Novel magnetic resonance imaging agents comprise complexes of paramagnetic ions with **hydrazide** derivs. of polyaminocarboxylic acid chelating agents. These novel imaging agents are characterized by excellent NMR image-contrasting properties and by high solubilities in physiol. solns. A novel method of performing an NMR diagnostic procedure involves administering to a warm-blooded animal an effective amt. of a complex as described above and then exposing the animal to an NMR imaging procedure, thereby imaging at least a portion of the body of the animal. The complex comprises the formula I, where  $\text{M}^{z+}$  is a paramagnetic ion of an element with an at. no. 21-29, 42-44, or 58-70 and a valence,  $z$ , of 2+ or 3+; A = II or III, where  $\text{R1} = \text{O}$  or IV, and  $\text{R1}$  group is IV;  $\text{R2-5} = \text{C1-6 alkyl, acyl, aryl, mono- or polyhydroxyalkyl, mono- or polyalkoxyalkyl, aminoalkyl, or acylaminoalkyl}$ ; R2 and R3 may be joined together to form a 5-, 6-, or 7-membered ring.

IT 143458-14-4P 143458-15-5P 143458-16-6P

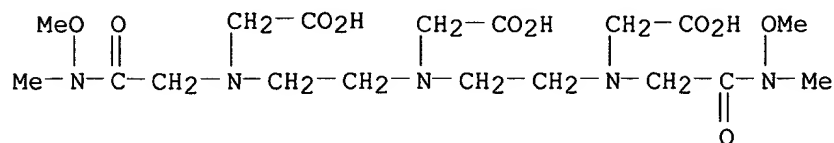
143481-68-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, for diagnostic magnetic resonance imaging of warm-blooded animals)

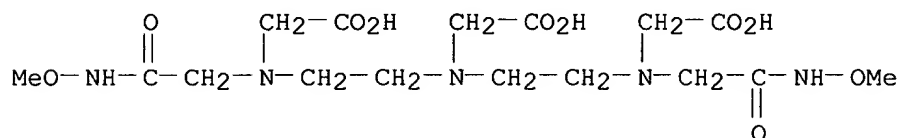
RN 143458-14-4 HCAPLUS

CN 2-Oxa-3,6,9,12-tetraazatetradecan-14-oic acid, 6,9-bis(carboxymethyl)-12-[2-(methoxymethylamino)-2-oxoethyl]-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



RN 143458-15-5 HCAPLUS

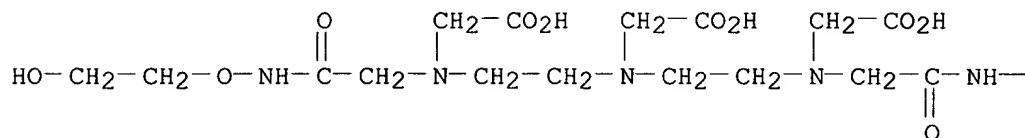
CN 2-Oxa-3,6,9,12-tetraazatetradecan-14-oic acid, 6,9-bis(carboxymethyl)-12-[2-(methoxyamino)-2-oxoethyl]-4-oxo- (9CI) (CA INDEX NAME)



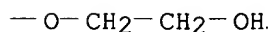
RN 143458-16-6 HCAPLUS

CN 3-Oxa-4,7,10,13-tetraazapentadecan-15-oic acid, 7,10-bis(carboxymethyl)-1-hydroxy-13-[2-[(2-hydroxyethoxy)amino]-2-oxoethyl]-5-oxo- (9CI) (CA INDEX NAME)

PAGE 1-A

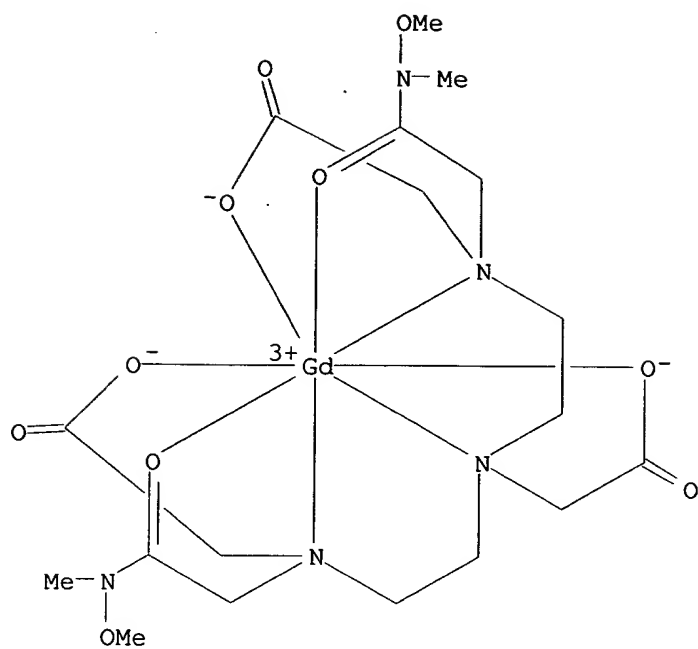


PAGE 1-B



RN 143481-68-9 HCAPLUS

CN Gadolinium, [6,9-bis(carboxymethyl)-12-[2-(methoxymethylamino)-2-oxoethyl]-3-methyl-4-oxo-2-oxa-3,6,9,12-tetraazatetradecan-14-oato(3-)]- (9CI) (CA INDEX NAME)



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L11 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1992:546344 HCAPLUS  
 DOCUMENT NUMBER: 117:146344  
 TITLE: Alkoxyamide-derivatized chelates for magnetic resonance imaging (MRI)  
 INVENTOR(S): **Rajagopalan, Raghavan**; Wallace, Rebecca A.; Periasamy, Muthanadar P.  
 PATENT ASSIGNEE(S): Mallinckrodt Medical, Inc., USA  
 SOURCE: PCT Int. Appl., 36 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9209884	A1	19920611	WO 1991-US8431	19911112
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9190810	A1	19920625	AU 1991-90810	19911112
AU 656355	B2	19950202		
JP 06502858	T2	19940331	JP 1992-501072	19911112
EP 660925	A1	19950705	EP 1992-902010	19911112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5217706	A	19930608	US 1992-893157	19920603
US 5314680	A	19940524	US 1993-12185	19930504
PRIORITY APPLN. INFO.:			US 1990-616459	19901121
			WO 1991-US8431	19911112
			US 1992-893157	19920603

OTHER SOURCE(S): MARPAT 117:146344

AB Complexes of paramagnetic ions with **hydrazide** derivs. of polyaminocarboxylic acid chelating agents are provided (Markush of various chelates included) for MRI agents, as are MRI diagnostic methods using the agents. Prepn. of selected MRI agents of the invention is included. Thus, methoxylamine-HCl was treated with methanolic NaOMe, and the product was further reacted with DTPA-dianhydride to form [N,N''-bis(N-methoxy)carbamoylmethyl]diethylenetriamine-N,N',N''-triacetic acid.

IT **7429-91-6D**, Dysprosium, chelates with polyaminocarboxylate **hydrazide** derivs. **7440-00-8D**, Neodymium, chelates with polyaminocarboxylate **hydrazide** derivs. **7440-52-0D**, Erbium, chelates with polyaminocarboxylate **hydrazide** derivs. **7440-54-2D**, Gadolinium, chelates with polyaminocarboxylate **hydrazide** derivs. **7440-60-0D**, Holmium, chelates with polyaminocarboxylate **hydrazide** derivs.  
 RL: BIOL (Biological study)  
 (for magnetic resonance imaging agents)

RN 7429-91-6 HCAPLUS

CN Dysprosium (8CI, 9CI) (CA INDEX NAME)

Dy

RN 7440-00-8 HCAPLUS

CN Neodymium (8CI, 9CI) (CA INDEX NAME)



Nd

RN 7440-52-0 HCAPLUS  
CN Erbium (8CI, 9CI) (CA INDEX NAME)

Er

RN 7440-54-2 HCAPLUS  
CN Gadolinium (8CI, 9CI) (CA INDEX NAME)

Gd

RN 7440-60-0 HCAPLUS  
CN Holmium (8CI, 9CI) (CA INDEX NAME)

Ho

IT 7439-95-4D, Magnesium, complexes 7440-23-5D, Sodium,  
complexes 7440-50-8D, Copper, complexes 7440-66-6D,  
Zinc, complexes 7440-70-2D, Calcium, complexes  
RL: BIOL (Biological study)  
(in magnetic resonance imaging compn. with chelate of paramagnetic ion  
with polyaminocarboxylate **hydrazide** deriv.)  
RN 7439-95-4 HCAPLUS  
CN Magnesium (8CI, 9CI) (CA INDEX NAME)

Mg

RN 7440-23-5 HCAPLUS  
CN Sodium (8CI, 9CI) (CA INDEX NAME)

Na

RN 7440-50-8 HCAPLUS  
CN Copper (7CI, 8CI, 9CI) (CA INDEX NAME)

Cu

RN 7440-66-6 HCAPLUS  
CN Zinc (7CI, 8CI, 9CI) (CA INDEX NAME)

Zn

RN 7440-70-2 HCAPLUS

CN Calcium (8CI, 9CI) (CA INDEX NAME)

Ca

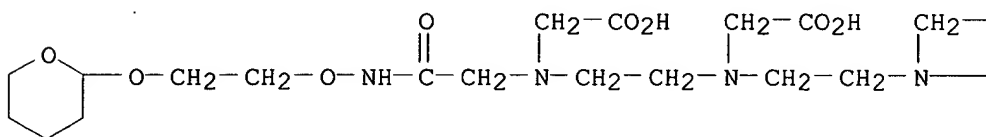
IT 143458-18-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and deblocking of, in chelating agent prepn. for magnetic  
 resonance imaging agent prepn.)

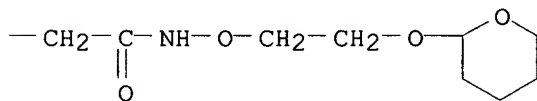
RN 143458-18-8 HCAPLUS

CN 3-Oxa-4,7,10,13-tetraazapentadecan-15-oic acid, 7,10-bis(carboxymethyl)-5-  
 oxo-13-[2-oxo-2-[[2-[(tetrahydro-2H-pyran-2-yl)oxy]ethoxy]amino]ethyl]-1-  
 [(tetrahydro-2H-pyran-2-yl)oxy]- (9CI) (CA INDEX NAME)

PAGE 1-A



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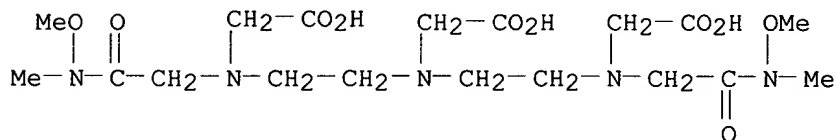
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IT 143458-14-4P 143458-15-5P 143458-16-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, for chelate for magnetic resonance imaging agent)

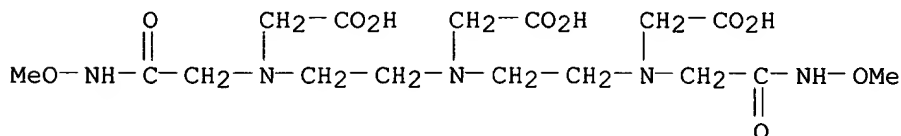
RN 143458-14-4 HCAPLUS

CN 2-Oxa-3,6,9,12-tetraazatetradecan-14-oic acid, 6,9-bis(carboxymethyl)-12-  
 [2-(methoxymethylamino)-2-oxoethyl]-3-methyl-4-oxo- (9CI) (CA INDEX NAME)



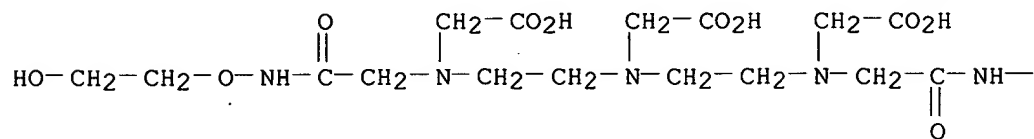
RN 143458-15-5 HCAPLUS

CN 2-Oxa-3,6,9,12-tetraazatetradecan-14-oic acid, 6,9-bis(carboxymethyl)-12-  
 [2-(methoxyamino)-2-oxoethyl]-4-oxo- (9CI) (CA INDEX NAME)

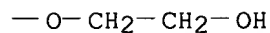


RN 143458-16-6 HCAPLUS  
 CN 3-Oxa-4,7,10,13-tetraazapentadecan-15-oic acid, 7,10-bis(carboxymethyl)-1-hydroxy-13-[2-[(2-hydroxyethoxy)amino]-2-oxoethyl]-5-oxo- (9CI) (CA INDEX NAME)

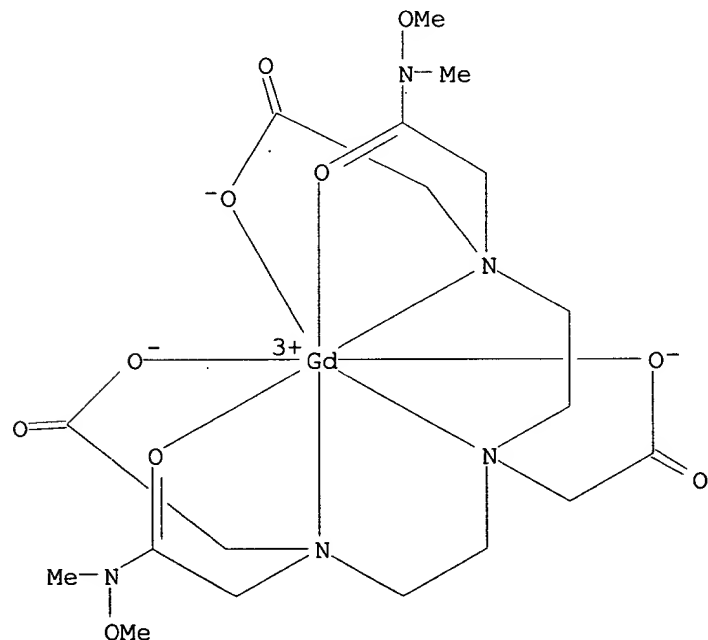
PAGE 1-A



PAGE 1-B



IT **143481-68-9P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, for magnetic resonance imaging agent)  
 RN 143481-68-9 HCAPLUS  
 CN Gadolinium, [6,9-bis(carboxymethyl)-12-[2-(methoxymethylamino)-2-oxoethyl]-3-methyl-4-oxo-2-oxa-3,6,9,12-tetraazatetradecan-14-oato(3-)]- (9CI) (CA INDEX NAME)



IT **12064-62-9**, Gadolinium oxide  
 RL: RCT (Reactant)  
 (reaction of, in chelate prepn. for magnetic resonance imaging agent)  
 RN 12064-62-9 HCAPLUS

CN Gadolinium oxide (Gd<sub>2</sub>O<sub>3</sub>) (8CI, 9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

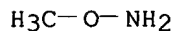
IT 593-56-6, Methoxylamine hydrochloride 6638-79-5  
23911-26-4 143458-17-7

RL: RCT (Reactant)

(reaction of, in chelating agent prepn. for magnetic resonance imaging agent prepn.)

RN 593-56-6 HCAPLUS

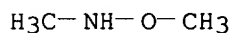
CN Hydroxylamine, O-methyl-, hydrochloride (8CI, 9CI) (CA INDEX NAME)



● HCl

RN 6638-79-5 HCAPLUS

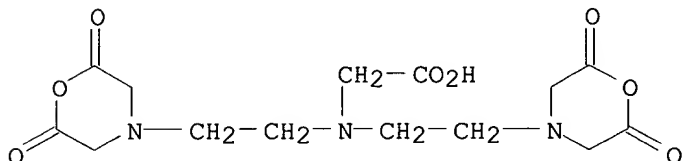
CN Methanamine, N-methoxy-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

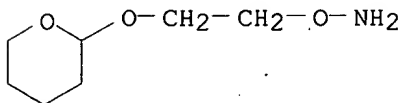
RN 23911-26-4 HCAPLUS

CN Glycine, N,N-bis[2-(2,6-dioxo-4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 143458-17-7 HCAPLUS

CN Hydroxylamine, O-[2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]- (9CI) (CA INDEX NAME)



IT 7439-89-6D, Iron, chelates with polyaminocarboxylate hydrazide derivs. 7439-96-5D, Manganese, chelates with polyaminocarboxylate hydrazide derivs. 7440-10-0D, Praseodymium, chelates with polyaminocarboxylate hydrazide derivs. 7440-19-9D, Samarium, chelates with polyaminocarboxylate hydrazide derivs. 7440-27-9D, Terbium, chelates with polyaminocarboxylate hydrazide derivs. 7440-64-4D,

Ytterbium, chelates with polyaminocarboxylate **hydrazide** derivs.  
 RL: BIOL (Biological study)  
 (trivalent, for magnetic resonance imaging agents)

RN 7439-89-6 HCAPLUS  
 CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

RN 7439-96-5 HCAPLUS  
 CN Manganese (8CI, 9CI) (CA INDEX NAME)

Mn

RN 7440-10-0 HCAPLUS  
 CN Praseodymium (8CI, 9CI) (CA INDEX NAME)

Pr

RN 7440-19-9 HCAPLUS  
 CN Samarium (8CI, 9CI) (CA INDEX NAME)

Sm

RN 7440-27-9 HCAPLUS  
 CN Terbium (8CI, 9CI) (CA INDEX NAME)

Tb

RN 7440-64-4 HCAPLUS  
 CN Ytterbium (8CI, 9CI) (CA INDEX NAME)

Yb

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L11 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:485989 HCAPLUS

DOCUMENT NUMBER: 117:85989

TITLE: Novel magnetic resonance imaging agents

INVENTOR(S): Rajagopalan, Raghavan; Vanderipe, Donald R.

PATENT ASSIGNEE(S): Mallinckrodt Medical, Inc., USA

SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

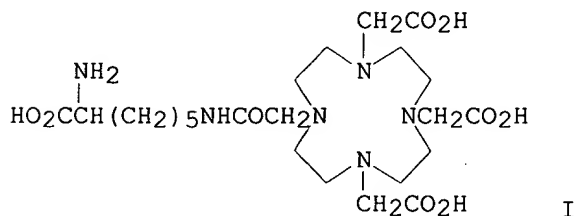
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9204919	A1	19920402	WO 1991-US6531	19910910
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5162109	A	19921110	US 1990-581861	19900913
CA 2068424	AA	19920314	CA 1991-2068424	19910910
AU 9188515	A1	19920415	AU 1991-88515	19910910
EP 500919	A1	19920902	EP 1991-918510	19910910
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05503107	T2	19930527	JP 1991-517858	19910910
PRIORITY APPLN. INFO.:			US 1990-581861	19900913
			WO 1991-US6531	19910910

OTHER SOURCE(S): MARPAT 117:85989

GI



AB MRI imaging agents comprising a zwitterionic complex of a paramagnetic ion having a cyclic or open chain structure are prepd. Aminopentyl-EDTA [H<sub>2</sub>N(CH<sub>2</sub>)<sub>5</sub>CH[N(CH<sub>2</sub>CO<sub>2</sub>H)<sub>2</sub>CH<sub>2</sub>N(CH<sub>2</sub>CO<sub>2</sub>H)<sub>2</sub>] was prepd. and complexed with Gd. [[(7-Aminoheptyl)imino]bisethylenenitrilo]]tetraacetic acid and I were also prepd. as ligands.

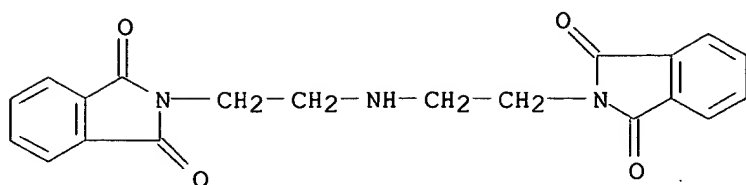
IT 63563-83-7

RL: RCT (Reactant)

(1substitution reaction of, with bromohexyl cyanide)

RN 63563-83-7 HCAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2,2'-(iminodi-2,1-ethanediyl)bis- (9CI) (CA INDEX NAME)



IT 7429-91-6D, Dysprosium, iminoacetate complexes 7439-89-6D  
 , Iron, iminoacetate complexes 7439-96-5D, Manganese,  
 iminoacetate complexes  
 RL: BIOL (Biological study)  
 (MRI imaging agents)  
 RN 7429-91-6 HCAPLUS  
 CN Dysprosium (8CI, 9CI) (CA INDEX NAME)

Dy

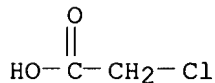
RN 7439-89-6 HCAPLUS  
 CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

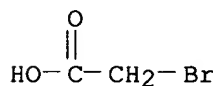
RN 7439-96-5 HCAPLUS  
 CN Manganese (8CI, 9CI) (CA INDEX NAME)

Mn

IT 79-11-8, Chloroacetic acid, reactions  
 RL: RCT (Reactant)  
 (alkylation by, of cyanoethylbis(aminoethyl)amine)  
 RN 79-11-8 HCAPLUS  
 CN Acetic acid, chloro- (8CI, 9CI) (CA INDEX NAME)



IT 79-08-3, Bromoacetic acid  
 RL: RCT (Reactant)  
 (alkylation by, of diaminoheptanenitrile)  
 RN 79-08-3 HCAPLUS  
 CN Acetic acid, bromo- (8CI, 9CI) (CA INDEX NAME)

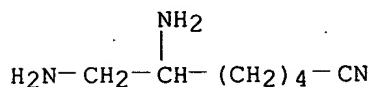


IT 142958-09-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and alkylation of, with bromoacetic acid)

RN 142958-09-6 HCAPLUS

CN Heptanenitrile, 6,7-diamino- (9CI) (CA INDEX NAME)

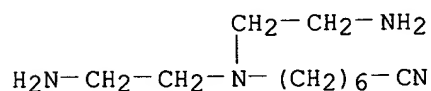


IT 103784-61-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and alkylation of, with chloroacetic acid)

RN 103784-61-8 HCAPLUS

CN Heptanenitrile, 7-[bis(2-aminoethyl)amino]- (9CI) (CA INDEX NAME)

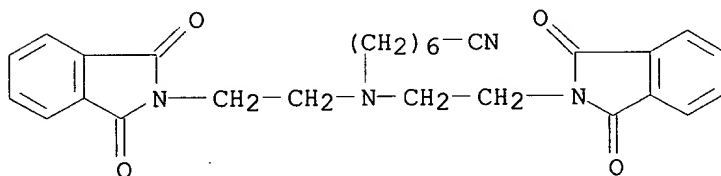


IT 103784-60-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and hydrazinolysis of)

RN 103784-60-7 HCAPLUS

CN Heptanenitrile, 7-[bis[2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)ethyl]amino]- (9CI) (CA INDEX NAME)

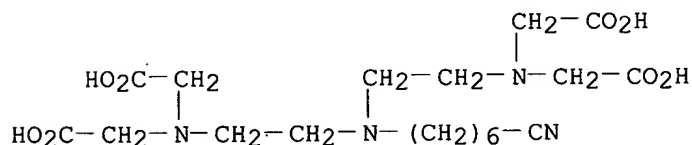


IT 103784-62-9P 142958-08-5P 142958-10-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and hydrogenation of)

RN 103784-62-9 HCAPLUS

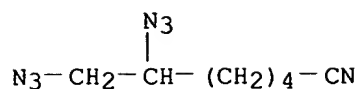
CN Glycine, N,N'-[[[(6-cyanoethyl)imino]di-2,1-ethanediyl]bis[N-(carboxymethyl)- (9CI) (CA INDEX NAME)



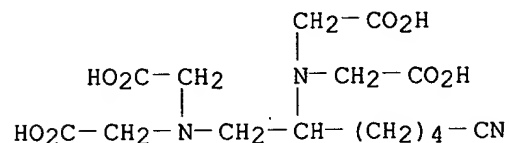
RN 142958-08-5 HCAPLUS

CN Heptanenitrile, 6,7-diazido- (9CI) (CA INDEX NAME)



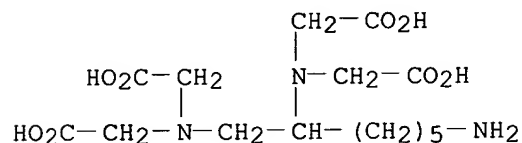


RN 142958-10-9 HCAPLUS  
 CN Glycine, N,N'-[1-(4-cyanobutyl)-1,2-ethanediyl]bis[N-(carboxymethyl)-  
 (9CI) (CA INDEX NAME)]



IT **142958-11-0P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

RN 142958-11-0 HCAPLUS  
 CN Glycine, N,N'-[1-(5-aminopentyl)-1,2-ethanediyl]bis[N-(carboxymethyl)-  
 (9CI) (CA INDEX NAME)]

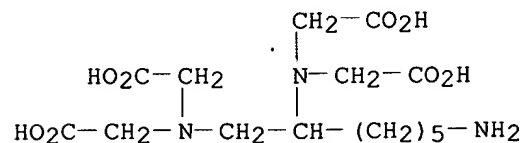


IT **7440-54-2DP**, Gadolinium, aminopentyl-EDTA complexes  
**142958-11-0DP**, gadolinium complexes  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as MRI imaging agent)

RN 7440-54-2 HCAPLUS  
 CN Gadolinium (8CI, 9CI) (CA INDEX NAME)

Gd

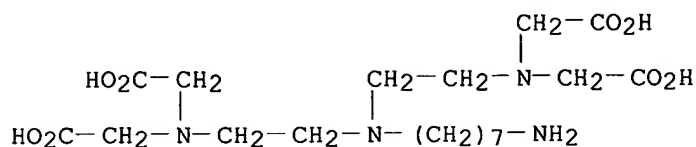
RN 142958-11-0 HCAPLUS  
 CN Glycine, N,N'-[1-(5-aminopentyl)-1,2-ethanediyl]bis[N-(carboxymethyl)-  
 (9CI) (CA INDEX NAME)]



IT **103784-63-0P 142958-12-1P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as ligand for MRI imaging complexes)

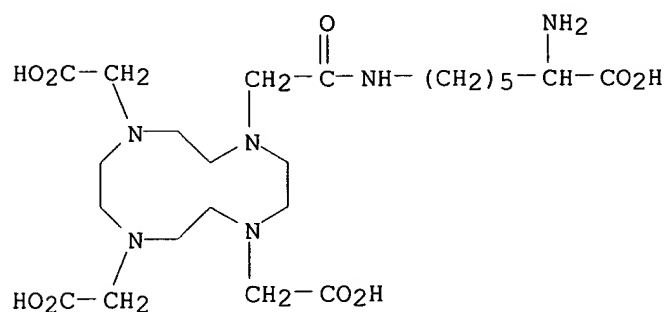
RN 103784-63-0 HCAPLUS

CN Glycine, N,N'-[[ (7-aminoheptyl)imino]di-2,1-ethanediyl]bis[N-(carboxymethyl)- (9CI) (CA INDEX NAME)



RN 142958-12-1 HCAPLUS

CN 1,4,7,10-Tetraazacyclododecane-1,4,7-triacetic acid, 10-[2-[(6-amino-6-carboxyhexyl)amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)



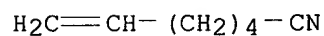
IT 5048-25-9, 6-Cyano-1-hexene

RL: RCT (Reactant)

(reaction of, with **azide**)

RN 5048-25-9 HCAPLUS

CN 6-Heptenenitrile (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



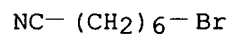
IT 20965-27-9

RL: RCT (Reactant)

(substitution reaction of, with bis(phthalimidoethyl)amine)

RN 20965-27-9 HCAPLUS

CN Heptanenitrile, 7-bromo- (6CI, 8CI, 9CI) (CA INDEX NAME)



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L11 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:687727 HCAPLUS

DOCUMENT NUMBER: 115:287727

TITLE: Synthesis and evaluation of the properties of  
fluorinated amphiphilic amides of 2,2-  
bis(hydroxymethyl)propionic acidAUTHOR(S): Selve, Claude; Delestre, Christine; **Achilefu,**  
**Samuel**; Maugras, Michel; Attiou, FatimaCORPORATE SOURCE: Lab. Etud. Solut. Org. Colloïdales, Univ. Nancy I,  
Vandoeuvre-les-Nancy, F 54506, Fr.SOURCE: J. Chem. Soc., Chem. Commun. (1991), (13), 863-4  
CODEN: JCCCAT; ISSN: 0022-4936

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The fluorinated amides synthesized are surfactants with negligible  
hemolytic effect and biol. aggressiveness to living cells.

IT 56602-33-6

RL: PRP (Properties)

(condensation of fluorinated amines with bis(hydroxymethyl)propionic  
acid in presence of)

RN 56602-33-6 HCAPLUS

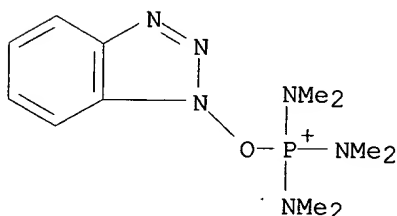
CN Phosphorus(1+), (1-hydroxy-1H-benzotriazolato-O)tris(N-  
methylethylmethanaminato)-, (T-4)-, hexafluorophosphate(1-) (9CI) (CA INDEX  
NAME)

CM 1

CRN 56602-32-5

CMF C12 H22 N6 O P

CDES 7:T-4

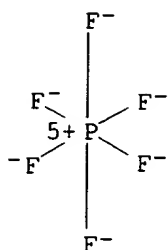


CM 2

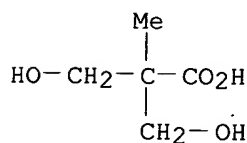
CRN 16919-18-9

CMF F6 P

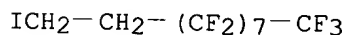
CCI CCS



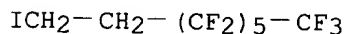
IT **4767-03-7**, 2,2-Bis(hydroxymethyl)propionic acid  
 RL: PRP (Properties)  
 (condensation of fluorinated amines with, in presence of  
 benzotriazol-yloxytris(dimethylamino)phosphonium hexafluorophosphate)  
 RN 4767-03-7 HCAPLUS  
 CN Propanoic acid, 3-hydroxy-2-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



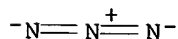
IT **2043-53-0 2043-57-4**  
 RL: PRP (Properties)  
 (nucleophilics substitution by **azide** ion and hydrogenation  
 and condensation with tertiary amine of)  
 RN 2043-53-0 HCAPLUS  
 CN Decane, 1,1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8-heptafluoro-10-iodo- (8CI, 9CI) (CA INDEX NAME)



RN 2043-57-4 HCAPLUS  
 CN Octane, 1,1,1,2,2,3,3,4,4,5,5,6,6-tridecafluoro-8-iodo- (7CI, 8CI, 9CI)  
 (CA INDEX NAME)



IT **14343-69-2, Azide**  
 RL: PRP (Properties)  
 (nucleophilics substitution of fluoroiodoethanes by, in prepn. of  
 fluorinated amides surfactant)  
 RN 14343-69-2 HCAPLUS  
 CN Azide (8CI, 9CI) (CA INDEX NAME)

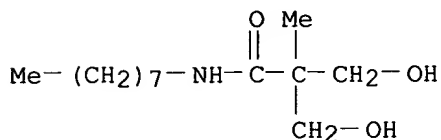


IT 137607-92-2P 137607-93-3P 137607-94-4P  
137607-95-5P 137607-96-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and surface tension and crit. micelle concn. for)

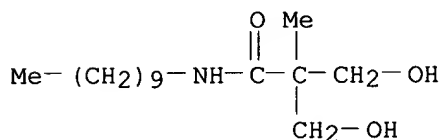
RN 137607-92-2 HCAPLUS

CN Propanamide, 3-hydroxy-2-(hydroxymethyl)-2-methyl-N-octyl- (9CI) (CA INDEX NAME)



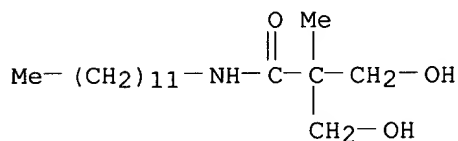
RN 137607-93-3 HCAPLUS

CN Propanamide, N-decyl-3-hydroxy-2-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



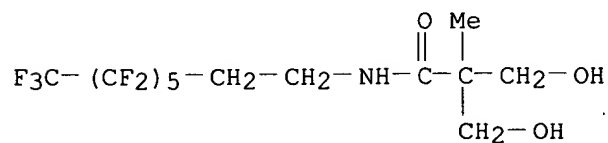
RN 137607-94-4 HCAPLUS

CN Propanamide, N-dodecyl-3-hydroxy-2-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



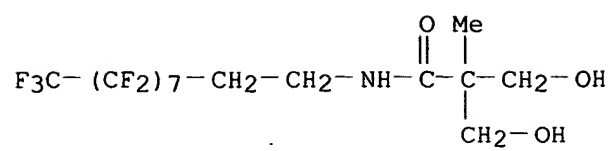
RN 137607-95-5 HCAPLUS

CN Propanamide, 3-hydroxy-2-(hydroxymethyl)-2-methyl-N-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)- (9CI) (CA INDEX NAME)



RN 137607-96-6 HCAPLUS

CN Propanamide, N-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptafluorodecyl)-3-hydroxy-2-(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



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L11 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1991:488414 HCAPLUS

DOCUMENT NUMBER: 115:88414

TITLE: **Hydrazide**-derivatized polyaminocarboxylic acid paramagnetic complexes as novel magnetic resonance imaging agentsINVENTOR(S): **Rajagopalan, Raghavan**

PATENT ASSIGNEE(S): Mallinckrodt, Inc., USA

SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9012598	A1	19901101	WO 1990-US1326	19900312
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 5384108	A	19950124	US 1989-341978	19890424
AU 9055350	A1	19901116	AU 1990-55350	19900312
AU 640140	B2	19930819		
EP 470188	A1	19920212	EP 1990-907933	19900312
EP 470188	B1	19940608		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 04507097	T2	19921210	JP 1990-508115	19900312
JP 3040462	B2	20000515		
AT 106751	E	19940615	AT 1990-907933	19900312
ES 2056465	T3	19941001	ES 1990-907933	19900312
PRIORITY APPLN. INFO.:			US 1989-341978	A 19890424
			EP 1990-907933	A 19900312
			WO 1990-US1326	A 19900312

OTHER SOURCE(S): MARPAT 115:88414

AB The title paramagnetic complexes, [(R1COCH2)2NAN(CH2COR1)2]M+z [A = CHR2CHR3, (CH2)2N(CH2COR1)(CH2)2; M+z = paramagnetic ion of element with at. no. = 21-23, 42-44, 58-70, and valence z = +2, +3; R1 = O-, N(R4)N(R5)R6; R4, R5, R6 = H, or C1-6 alkyl, hydroxyalkyl, alkoxyalkyl, aminoalkyl, or acylaminoalkyl; or NR5R6 or R4NNR5 = 5-, 6-, 7-member heterocycle (further defined); R2, R3 = H, C1-6 alkyl, Ph, Bz; 2-3 of R1 = O-] are magnetic resonance imaging agent having excellent NMR image-contrasting properties and high solys. in physiol. solns. Diagnostic compns. for enteral or parenteral administration are also disclosed. DTPA-dianhydride and N,N-dimethylhydrazine were reacted in iso-PrOH at 50.degree. to prep. a ligand which was reacted with Gd2O3 in H2O at 65-70.degree. to give [N,N'-bis(2,2-dimethylhydrazino)carbonylmethyl]diethylenetriamine-N,N',N''-triaceto]gadolinium(III) hydrate (I) in 88% yield. The LD50 of I in ICR mice was 11.5 mmol/kg. The relaxivity of I was 4.85 mM-1 s-1. A parenteral formulation contained Gd DTPA-bis(**hydrazide**) 330, Ca DTPA-bis(**hydrazide**) 14 mg/mL, and distd. H2O to 1 mL, pH 7.0.

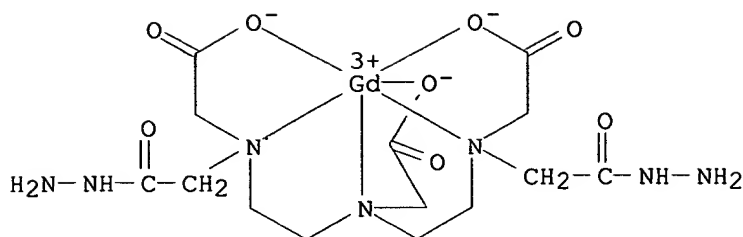
IT 135471-42-0

RL: BIOL (Biological study)

(as magnetic resonance imaging agent, parenteral formulation contg.)

RN 135471-42-0 HCAPLUS

CN Gadolinium, [N,N-bis[2-[(carboxymethyl)(2-hydrazino-2-oxoethyl)amino]ethyl]glycinato(3-)]- (9CI) (CA INDEX NAME)



IT 7439-95-4D, Magnesium, **hydrazide**-derivatized  
polyaminocarboxylic acid complexes 7440-66-6D, Zinc,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
7440-70-2D, Calcium, **hydrazide**-derivatized  
polyaminocarboxylic acid complexes  
RL: BIOL (Biological study)  
(diagnostic compn. contg. paramagnetic complex and, for magnetic  
resonance imaging)

RN 7439-95-4 HCAPLUS

CN Magnesium (8CI, 9CI) (CA INDEX NAME)

Mg

RN 7440-66-6 HCAPLUS

CN Zinc (7CI, 8CI, 9CI) (CA INDEX NAME)

Zn

RN 7440-70-2 HCAPLUS

CN Calcium (8CI, 9CI) (CA INDEX NAME)

Ca

IT 7429-91-6D, Dysprosium, **hydrazide**-derivatized  
polyaminocarboxylic acid complexes 7439-89-6D, Iron,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
7439-96-5D, Manganese, **hydrazide**-derivatized  
polyaminocarboxylic acid complexes 7439-98-7D, Molybdenum,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
7440-00-8D, Neodymium, **hydrazide**-derivatized  
polyaminocarboxylic acid complexes 7440-02-0D, Nickel,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
7440-10-0D, Praseodymium, **hydrazide**-derivatized  
polyaminocarboxylic acid complexes 7440-12-2D, Promethium,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
7440-18-8D, Ruthenium, **hydrazide**-derivatized  
polyaminocarboxylic acid complexes 7440-19-9D, Samarium,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
7440-20-2D, Scandium, **hydrazide**-derivatized  
polyaminocarboxylic acid complexes 7440-26-8D, Technetium,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes



7440-27-9D, Terbium, **hydrazide**-derivatized  
 polyaminocarboxylic acid complexes 7440-30-4D, Thulium,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
 7440-32-6D, Titanium, **hydrazide**-derivatized  
 polyaminocarboxylic acid complexes 7440-45-1D, Cerium,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
 7440-47-3D, Chromium, **hydrazide**-derivatized  
 polyaminocarboxylic acid complexes 7440-48-4D, Cobalt,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
 7440-50-8D, Copper, **hydrazide**-derivatized  
 polyaminocarboxylic acid complexes 7440-52-0D, Erbium,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
 7440-53-1D, Europium, **hydrazide**-derivatized  
 polyaminocarboxylic acid complexes 7440-54-2D, Gadolinium,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
 7440-60-0D, Holmium, **hydrazide**-derivatized  
 polyaminocarboxylic acid complexes 7440-62-2D, Vanadium,  
**hydrazide**-derivatized polyaminocarboxylic acid complexes  
 7440-64-4D, Ytterbium, **hydrazide**-derivatized  
 polyaminocarboxylic acid complexes  
 RL: BIOL (Biological study)

(paramagnetic, as magnetic resonance imaging agents)

RN 7429-91-6 HCAPLUS  
 CN Dysprosium (8CI, 9CI) (CA INDEX NAME)

Dy

RN 7439-89-6 HCAPLUS  
 CN Iron (7CI, 8CI, 9CI) (CA INDEX NAME)

Fe

RN 7439-96-5 HCAPLUS  
 CN Manganese (8CI, 9CI) (CA INDEX NAME)

Mn

RN 7439-98-7 HCAPLUS  
 CN Molybdenum (8CI, 9CI) (CA INDEX NAME)

Mo

RN 7440-00-8 HCAPLUS  
 CN Neodymium (8CI, 9CI) (CA INDEX NAME)

Nd

RN 7440-02-0 HCAPLUS  
 CN Nickel (8CI, 9CI) (CA INDEX NAME)

Ni

RN 7440-10-0 HCAPLUS  
CN Praseodymium (8CI, 9CI) (CA INDEX NAME)

Pr

RN 7440-12-2 HCAPLUS  
CN Promethium (8CI, 9CI) (CA INDEX NAME)

Pm

RN 7440-18-8 HCAPLUS  
CN Ruthenium (8CI, 9CI) (CA INDEX NAME)

Ru

RN 7440-19-9 HCAPLUS  
CN Samarium (8CI, 9CI) (CA INDEX NAME)

Sm

RN 7440-20-2 HCAPLUS  
CN Scandium (8CI, 9CI) (CA INDEX NAME)

Sc

RN 7440-26-8 HCAPLUS  
CN Technetium (8CI, 9CI) (CA INDEX NAME)

Tc

RN 7440-27-9 HCAPLUS  
CN Terbium (8CI, 9CI) (CA INDEX NAME)

Tb

RN 7440-30-4 HCAPLUS  
CN Thulium (8CI, 9CI) (CA INDEX NAME)

Tm

RN 7440-32-6 HCAPLUS  
CN Titanium (8CI, 9CI) (CA INDEX NAME)

Ti

RN 7440-45-1 HCAPLUS  
CN Cerium (8CI, 9CI) (CA INDEX NAME)

Ce

RN 7440-47-3 HCAPLUS  
CN Chromium (8CI, 9CI) (CA INDEX NAME)

Cr

RN 7440-48-4 HCAPLUS  
CN Cobalt (8CI, 9CI) (CA INDEX NAME)

Co

RN 7440-50-8 HCAPLUS  
CN Copper (7CI, 8CI, 9CI) (CA INDEX NAME)

Cu

RN 7440-52-0 HCAPLUS  
CN Erbium (8CI, 9CI) (CA INDEX NAME)

Er

RN 7440-53-1 HCAPLUS  
CN Europium (8CI, 9CI) (CA INDEX NAME)

Eu

RN 7440-54-2 HCAPLUS  
CN Gadolinium (8CI, 9CI) (CA INDEX NAME)

Gd

RN 7440-60-0 HCAPLUS  
CN Holmium (8CI, 9CI) (CA INDEX NAME)

Ho

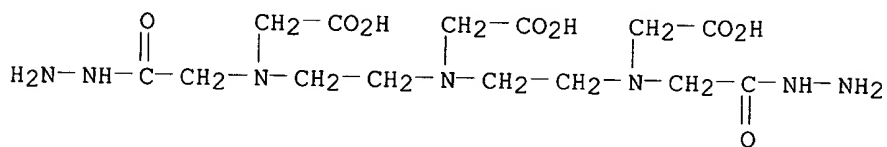
RN 7440-62-2 HCAPLUS  
 CN Vanadium (8CI, 9CI) (CA INDEX NAME)

V

RN 7440-64-4 HCAPLUS  
 CN Ytterbium (8CI, 9CI) (CA INDEX NAME)

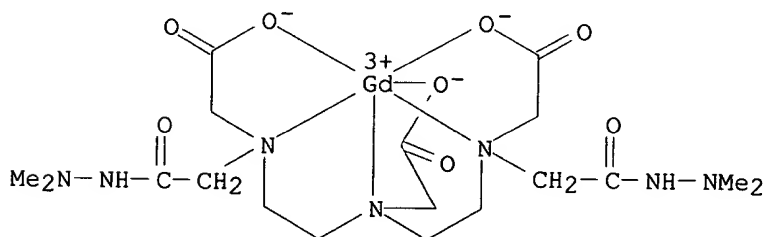
Yb

IT **135589-99-0**  
 RL: BIOL (Biological study)  
 (parenteral magnetic resonance imaging agent formulation contg.  
 gadolinium complex and)  
 RN 135589-99-0 HCAPLUS  
 CN Glycine, N,N-bis[2-[(carboxymethyl)(2-hydrazino-2-oxoethyl)amino]ethyl]-,  
 calcium salt (2:3) (9CI) (CA INDEX NAME)



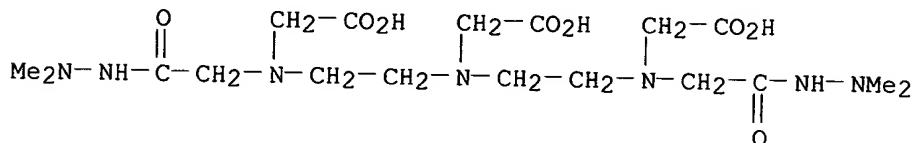
● 3/2 Ca

IT **135443-51-5P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, as magnetic resonance imaging agent)  
 RN 135443-51-5 HCAPLUS  
 CN Gadolinium, [6,9-bis(carboxymethyl)-12-[2-(2,2-dimethylhydrazino)-2-oxoethyl]-2-methyl-4-oxo-2,3,6,9,12-pentaazatetradecan-14-oato(3-)-N6,N9,N12,O6,O9,O14]- (9CI) (CA INDEX NAME)



IT **135589-98-9P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of, in prepn. of paramagnetic complex for magnetic resonance

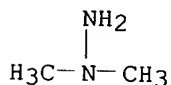
imaging)  
 RN 135589-98-9 HCAPLUS  
 CN 2,3,6,9,12-Pentaazatetradecan-14-oic acid, 6,9-bis(carboxymethyl)-12-[2-(2,2-dimethylhydrazino)-2-oxoethyl]-2-methyl-4-oxo- (9CI) (CA INDEX NAME)



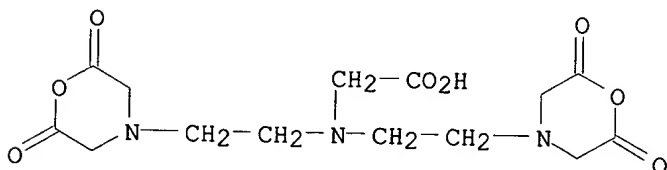
IT 12064-62-9, Gadolinium oxide  
 RL: RCT (Reactant)  
 (reaction of, in prepn. of magnetic resonance imaging agent)  
 RN 12064-62-9 HCAPLUS  
 CN Gadolinium oxide (Gd2O3) (8CI, 9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 57-14-7, N,N-Dimethylhydrazine  
 RL: RCT (Reactant)  
 (reaction of, with DTPA-dianhydride, in prepn. of paramagnetic complex)  
 RN 57-14-7 HCAPLUS  
 CN Hydrazine, 1,1-dimethyl- (8CI, 9CI) (CA INDEX NAME)



IT 23911-26-4  
 RL: RCT (Reactant)  
 (reaction of, with dimethylhydrazine, in prepn. of paramagnetic complex)  
 RN 23911-26-4 HCAPLUS  
 CN Glycine, N,N-bis[2-(2,6-dioxo-4-morpholinyl)ethyl]- (9CI) (CA INDEX NAME)



# Inventor Search

CEPERLEY 09/898,885

=> d que 114

L1 345 SEA FILE=HCAPLUS ABB=ON PLU=ON RAJAGOPALAN R?/AU  
L2 49 SEA FILE=HCAPLUS ABB=ON PLU=ON BUGAJ J?/AU  
L3 48 SEA FILE=HCAPLUS ABB=ON PLU=ON DORSHOW R?/AU  
L4 44 SEA FILE=HCAPLUS ABB=ON PLU=ON ACHILEFU S?/AU  
L5 415 SEA FILE=HCAPLUS ABB=ON PLU=ON (L1 OR L2 OR L3 OR L4) *focus on*  
L8 16 SEA FILE=HCAPLUS ABB=ON PLU=ON L5 AND PHOTO?  
L9 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L8 AND DYE?  
L12 64 SEA FILE=REGISTRY ABB=ON PLU=ON (302794-43-0/BI OR 83150-76-9  
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309916-88-9/BI OR 309916-89-0/BI OR 309916-90-3/BI OR 115239-21  
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-4/BI OR 411241-19-5/BI OR 411241-20-8/BI OR 4701-17-1/BI OR  
51110-01-1/BI OR 51992-85-9/BI OR 59090-17-4/BI OR 6318-16-7/BI  
OR 64-17-5/BI OR 9011-97-6/BI)  
L13 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 AND L9  
L14 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L13 OR L9

=&gt; d ibib abs hitstr 1

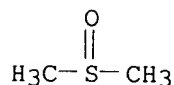
L14 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:294120 HCAPLUS  
 DOCUMENT NUMBER: 136:306089  
 TITLE: Tumor-targeted optical contrast agents  
 INVENTOR(S): Achilefu, Samuel I.; Rajagopalan,  
 Raghavan; Dorshow, Richard B.;  
 Bugaj, Joseph E.  
 PATENT ASSIGNEE(S): Mallinckrodt Inc., USA  
 SOURCE: U.S. Pat. Appl. Publ., 31 pp., Cont.-in-part of U.S.  
 Ser. No. 484,320.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002044909	A1	20020418	US 2001-863971	20010523
PRIORITY APPLN. INFO.: US 2000-484320			A2	20000118

AB Cyanine **dye** bioconjugates useful for diagnostic imaging and therapy are disclosed. The conjugates include several cyanine **dyes** with a variety of bis- and tetrakis (carboxylic acid) homologs. The compds. may be conjugated to bioactive peptides, carbohydrates, hormones, drugs, or other bioactive agents. The small size of the compds. allows more favorable delivery to tumor cells as compared to larger mol. wt. imaging agents. The various **dyes** are useful over the range of 350 to 1,300 nm, the exact range being dependent upon the particular **dye**. The use of dimethylsulfoxide helps to maintain the fluorescence of the compds. The inventive compds. are useful for diagnostic imaging and therapy, in endoscopic applications for the detection of tumors and other abnormalities, for localized therapy, for **photoacoustic** tumor imaging, detection and therapy, and for sonofluorescence tumor imaging, detection and therapy.

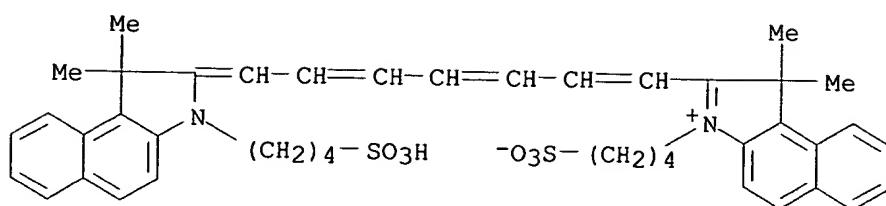
IT 67-68-5, DMSO, biological studies  
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (DMSO formulation for cyanine **dye**-peptide conjugates used as tumor-targeted optical contrast agents)

RN 67-68-5 HCAPLUS  
 CN Methane, sulfinylbis- (9CI) (CA INDEX NAME)



IT 3599-32-4, Indocyanine green 31362-50-2D, Bombesin, cyanine **dye** conjugates  
 RL: DGN (Diagnostic use); BIOL (Biological study); USES (Uses)  
 (cyanine **dye**-peptide conjugates as tumor-targeted optical contrast agents)

RN 3599-32-4 HCAPLUS  
 CN 1H-Benz[e]indolium, 2-[7-[1,3-dihydro-1,1-dimethyl-3-(4-sulfobutyl)-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-3-(4-sulfobutyl)-, inner salt, sodium salt (9CI) (CA INDEX NAME)

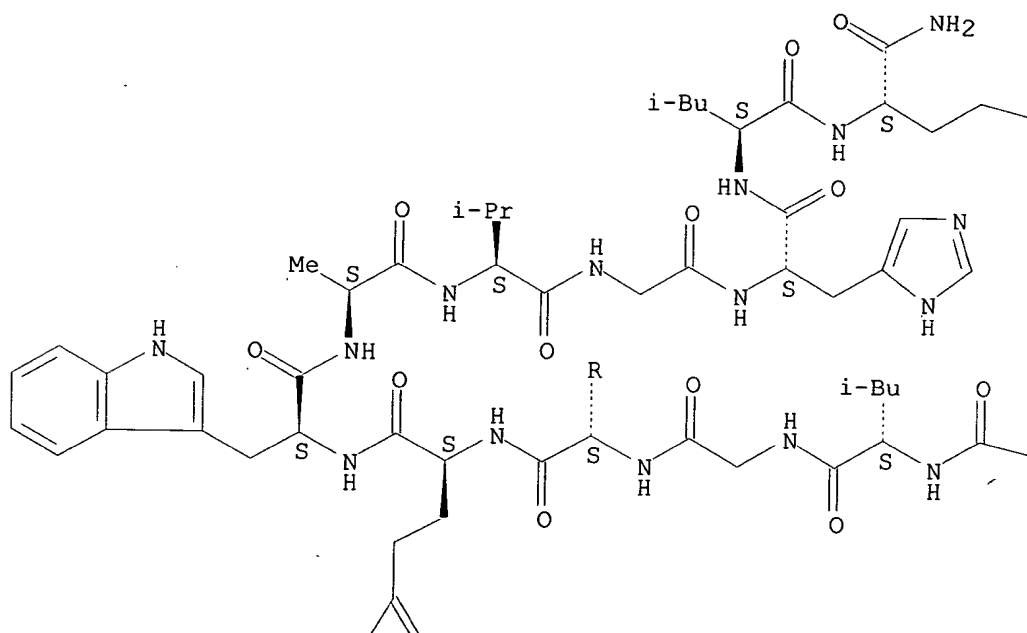


● Na

RN 31362-50-2 HCAPLUS  
CN Bombesin (9CI) (CA INDEX NAME)

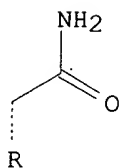
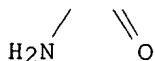
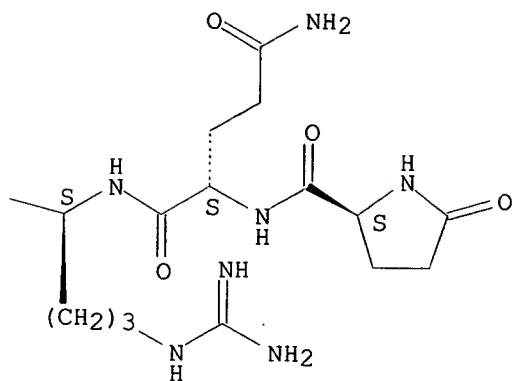
Absolute stereochemistry.

PAGE 1-A



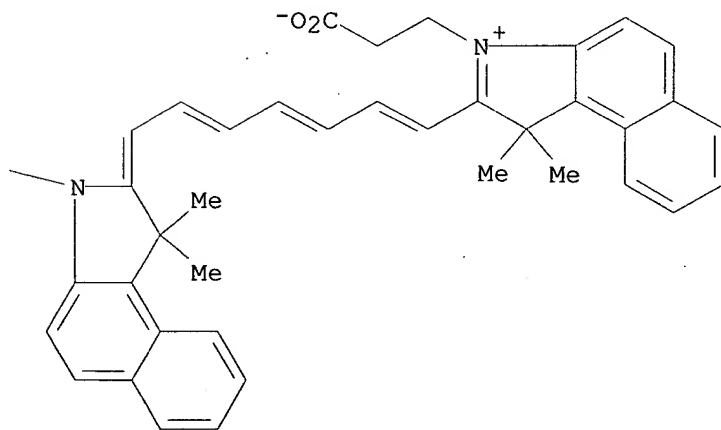
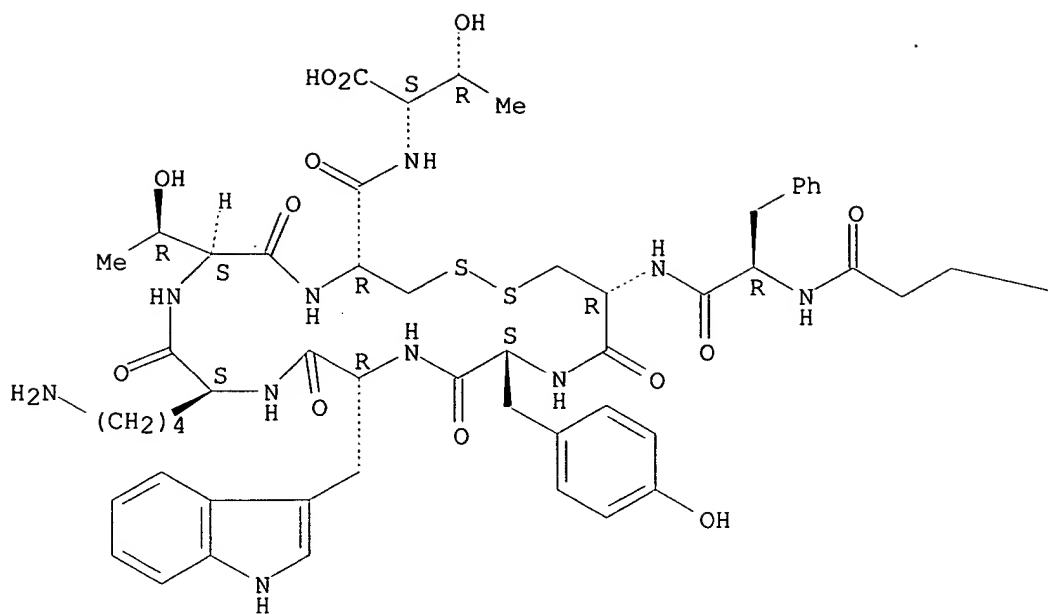


— SMe



IT 411241-16-2P 411241-17-3P 411241-20-8P  
 RL: DGN (Diagnostic use); PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses) (cyanine **dye**-peptide conjugates as tumor-targeted optical contrast agents)  
 RN 411241-16-2 HCAPLUS  
 CN INDEX NAME NOT YET ASSIGNED

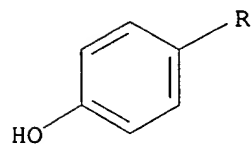
Absolute stereochemistry.  
 Double bond geometry unknown.



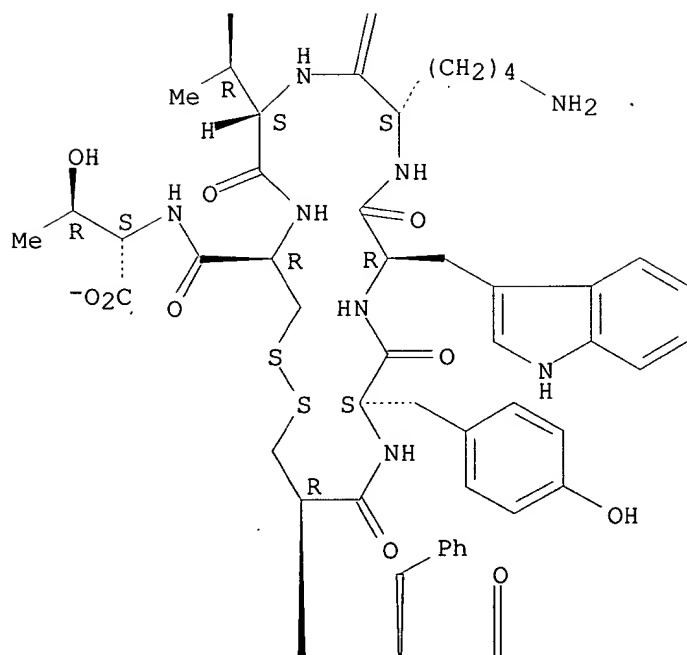
RN 411241-17-3 HCAPLUS  
 CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.  
 Double bond geometry unknown.

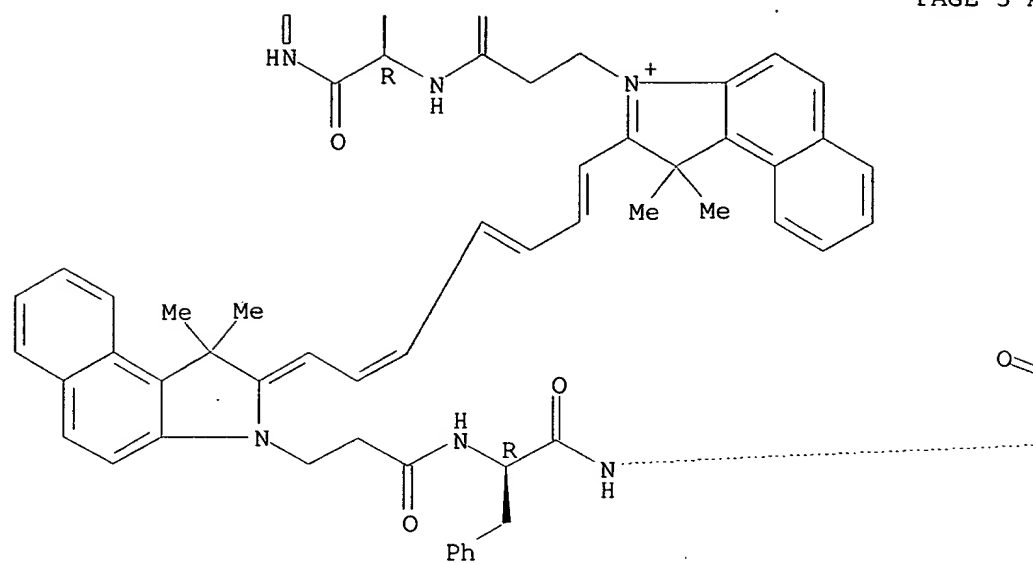
PAGE 1-A



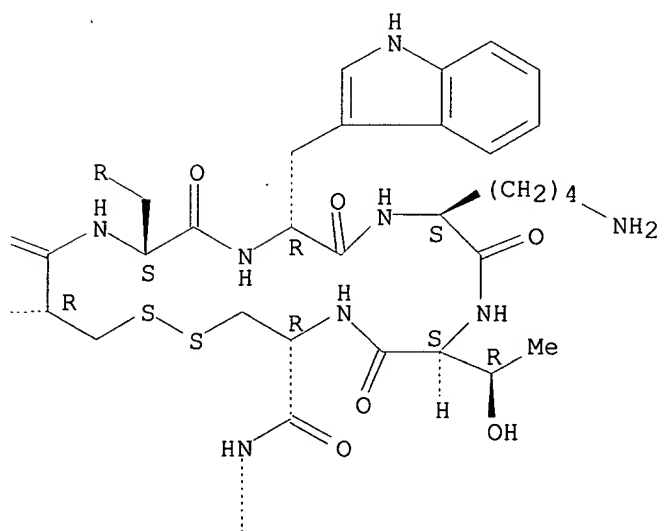
PAGE 2-A



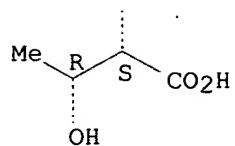
PAGE 3-A



PAGE 3-B



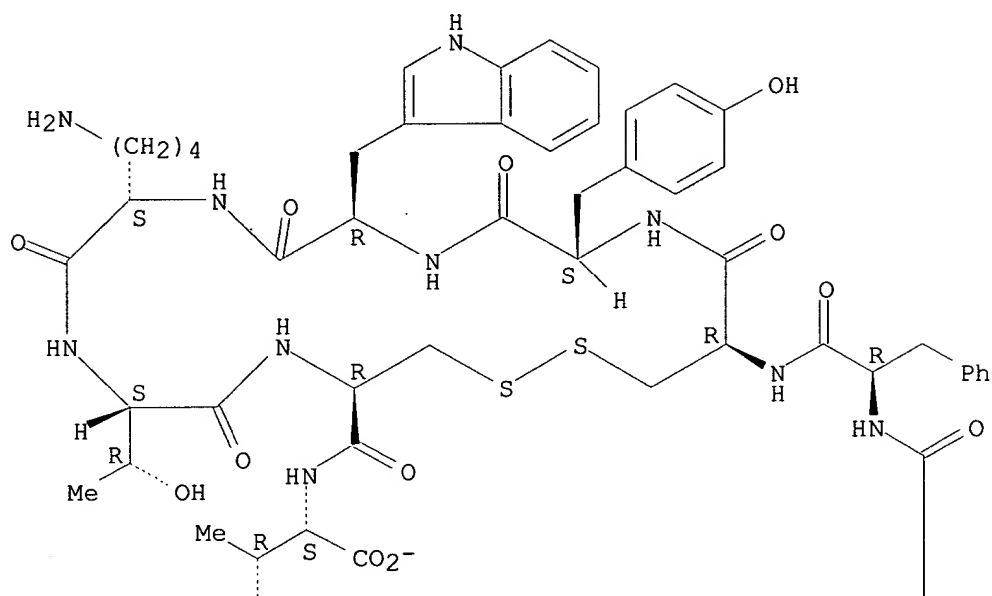
PAGE 4-B



RN 411241-20-8 HCAPLUS  
CN INDEX NAME NOT YET ASSIGNED

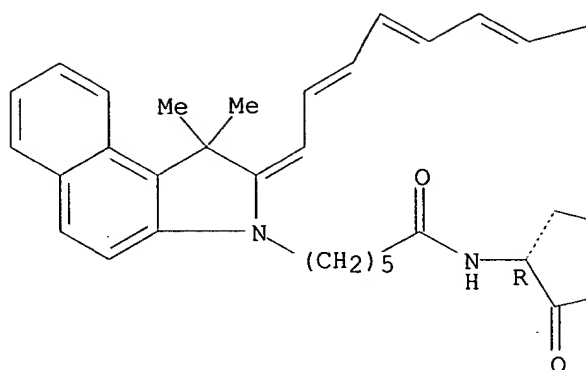
Absolute stereochemistry.  
Double bond geometry unknown.

PAGE 1-A

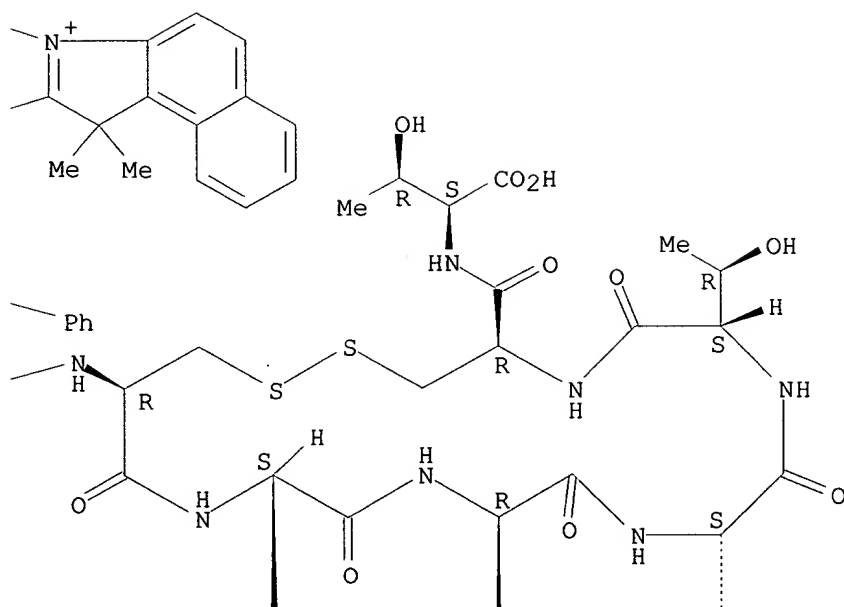


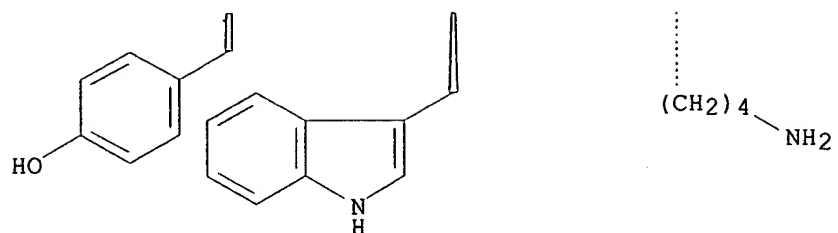
OH

PAGE 2-A  
|  
(CH<sub>2</sub>)<sub>5</sub>



PAGE 2-B





IT 411241-19-5P

RL: DGN (Diagnostic use); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(cyanine **dye**-peptide conjugates as tumor-targeted optical contrast agents)

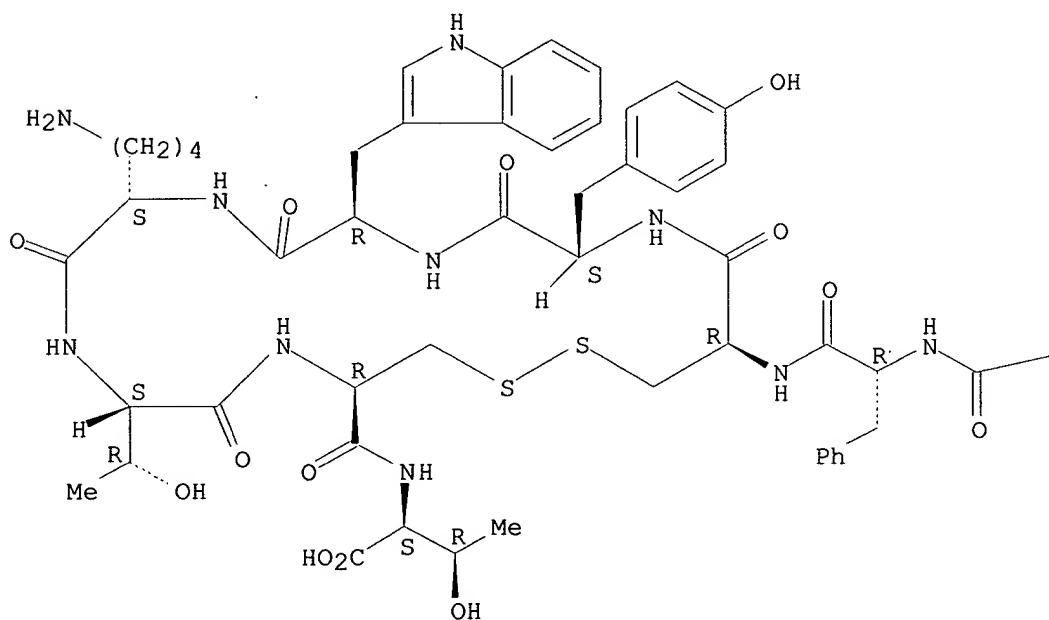
RN 411241-19-5 HCAPLUS

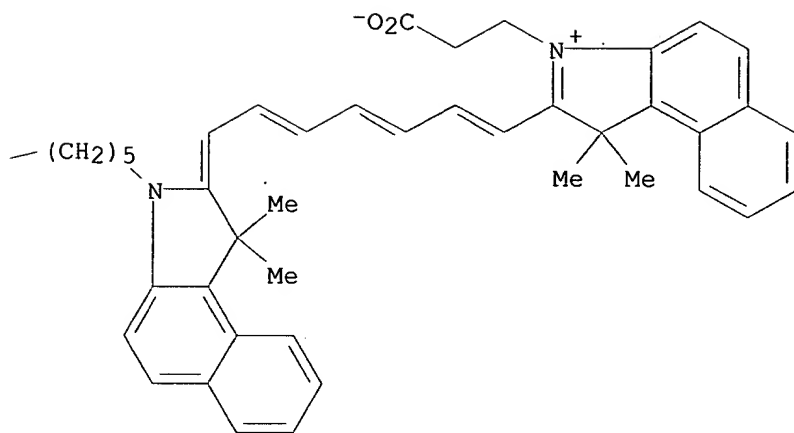
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.

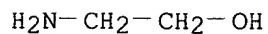
Double bond geometry unknown.

PAGE 1-A

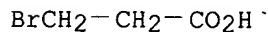




IT 141-43-5, Ethanolamine, reactions 590-92-1,  
 3-Bromopropanoic acid 1640-39-7, 2,3,3-Trimethylindole  
 2531-70-6 4224-70-8, 6-Bromohexanoic acid  
 5437-45-6, Benzyl bromoacetate 41532-84-7,  
 1,1,2-Trimethyl[1H]benz[e]indole 59090-17-4, Glutaconaldehyde  
 dianil 61010-04-6 65476-32-6, 4-  
 Carboxymethylphenylhydrazine hydrochloride 83150-76-9,  
 Octreotide 302794-43-0 411241-11-7 411241-14-0  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (cyanine **dye**-peptide conjugates as tumor-targeted optical  
 contrast agents)  
 RN 141-43-5 HCAPLUS  
 CN Ethanol, 2-amino- (8CI, 9CI) (CA INDEX NAME)

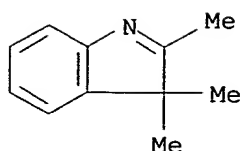


RN 590-92-1 HCAPLUS  
 CN Propanoic acid, 3-bromo- (9CI) (CA INDEX NAME)

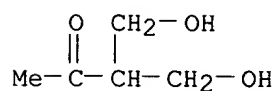


RN 1640-39-7 HCAPLUS  
 CN 3H-Indole, 2,3,3-trimethyl- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

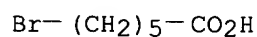




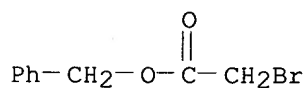
RN 2531-70-6 HCAPLUS  
CN 2-Butanone, 4-hydroxy-3-(hydroxymethyl)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



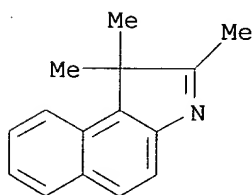
RN 4224-70-8 HCAPLUS  
CN Hexanoic acid, 6-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



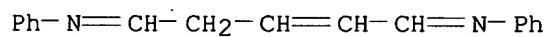
RN 5437-45-6 HCAPLUS  
CN Acetic acid, bromo-, phenylmethyl ester (9CI) (CA INDEX NAME)



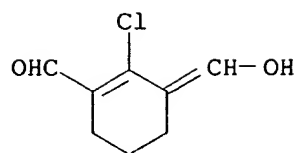
RN 41532-84-7 HCAPLUS  
CN 1H-Benz[e]indole, 1,1,2-trimethyl- (9CI) (CA INDEX NAME)



RN 59090-17-4 HCAPLUS  
CN Benzenamine, N,N'-2-pentene-1,5-diylidenebis- (9CI) (CA INDEX NAME)

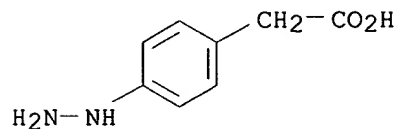


RN 61010-04-6 HCAPLUS  
CN 1-Cyclohexene-1-carboxaldehyde, 2-chloro-3-(hydroxymethylene)- (9CI) (CA INDEX NAME)



RN 65476-32-6 HCAPLUS

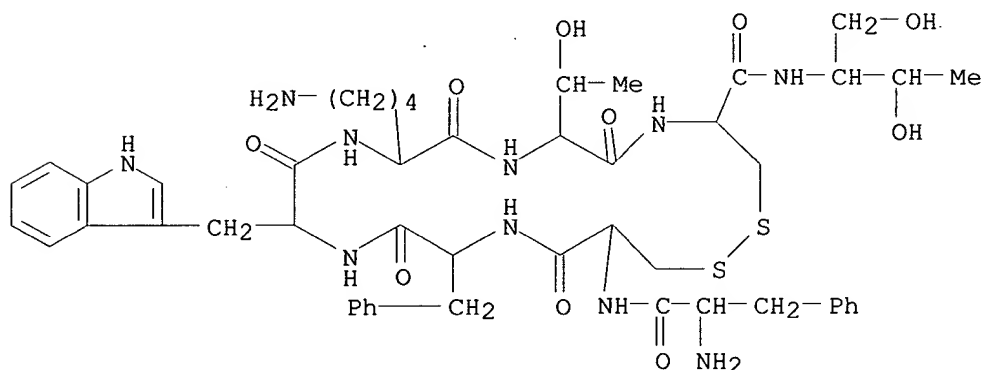
CN Benzeneacetic acid, 4-hydrazino-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

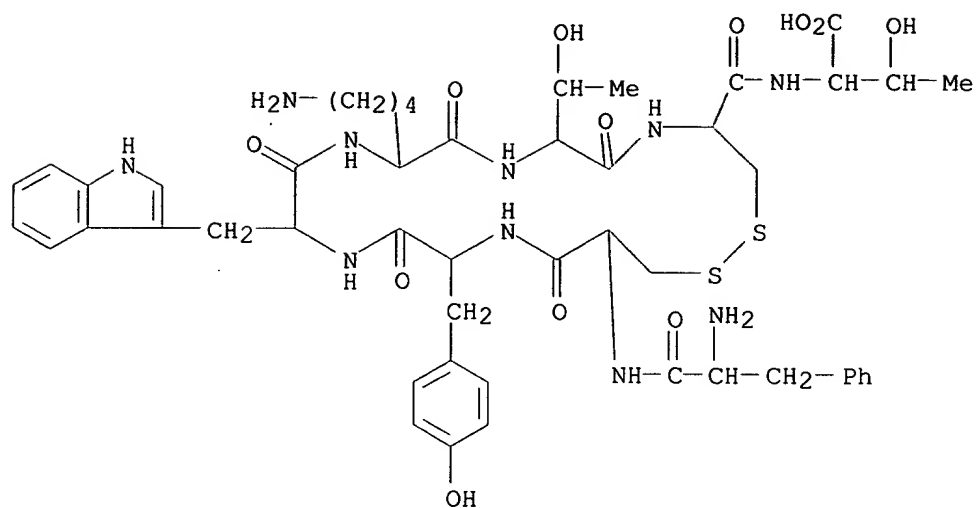
RN 83150-76-9 HCAPLUS

CN L-Cysteinamide, D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)



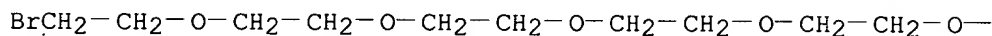
RN 302794-43-0 HCAPLUS

CN L-Threonine, D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)

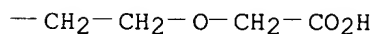


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CN INDEX NAME NOT YET ASSIGNED

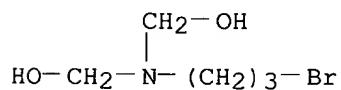
PAGE 1-A



PAGE 1-B



RN 411241-14-0 HCAPLUS  
CN Methanol, [(3-bromopropyl)imino]bis- (9CI) (CA INDEX NAME)

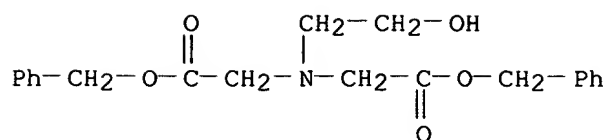


IT 51992-85-9P 146432-42-0P 351439-68-4P  
411241-12-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
(Reactant or reagent)  
(cyanine **dye**-peptide conjugates as tumor-targeted optical  
contrast agents)

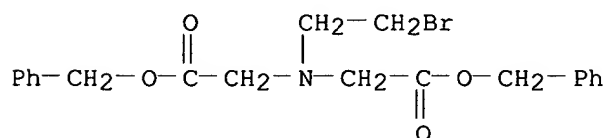
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CN Glycine, N-(2-hydroxyethyl)-N-[2-oxo-2-(phenylmethoxy)ethyl]-,  
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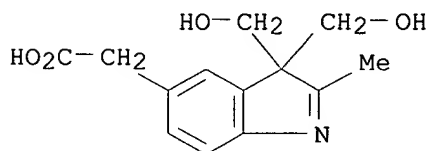
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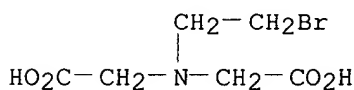
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CN 3H-Indole-5-acetic acid, 3,3-bis(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



RN 411241-12-8 HCAPLUS

CN Glycine, N-(2-bromoethyl)-N-(carboxymethyl)- (9CI) (CA INDEX NAME)



IT 25126-32-3DP, Cholecystokinin-8 (swine), analogs

25679-24-7P 31362-50-2DP, Bombesin, analogs

39379-15-2DP, Neurotensin, analogs 95781-56-9P

95837-47-1P 105466-87-3P 115239-21-9P

195825-84-4P 309916-88-9P 309916-89-0P

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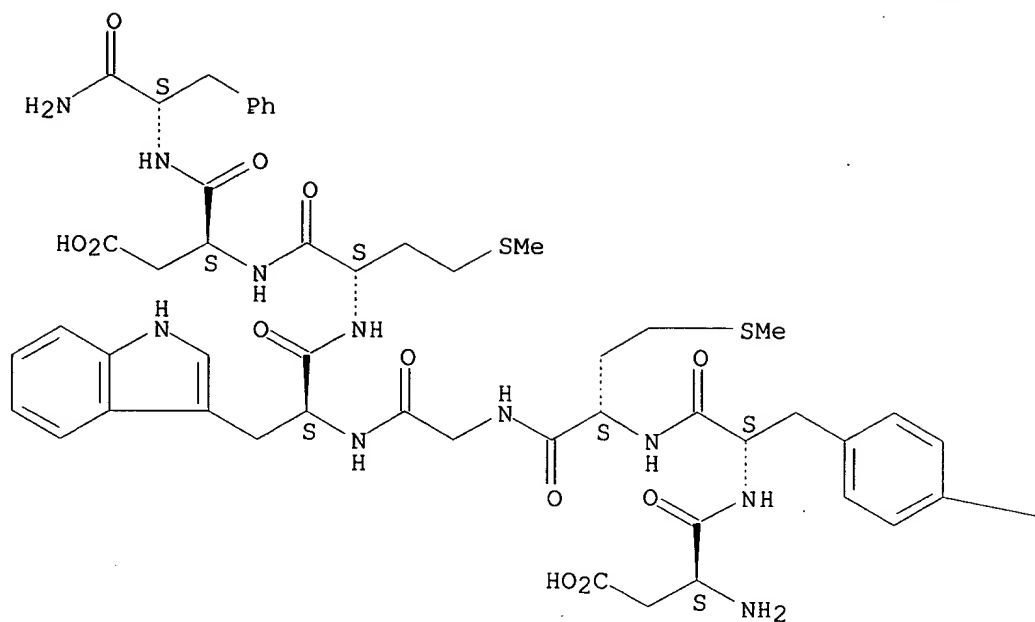
RL: SPN (Synthetic preparation); PREP (Preparation)

(cyanine **dye**-peptide conjugates as tumor-targeted optical contrast agents)

RN 25126-32-3 HCAPLUS

CN Cholecystokinin-8 (swine) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

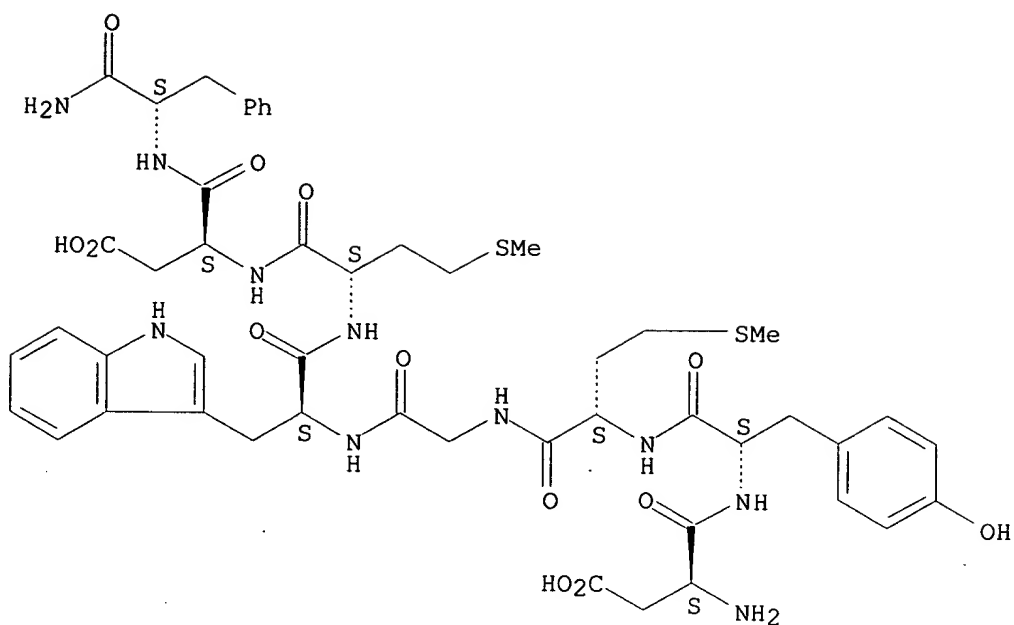


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RN 25679-24-7 HCAPLUS

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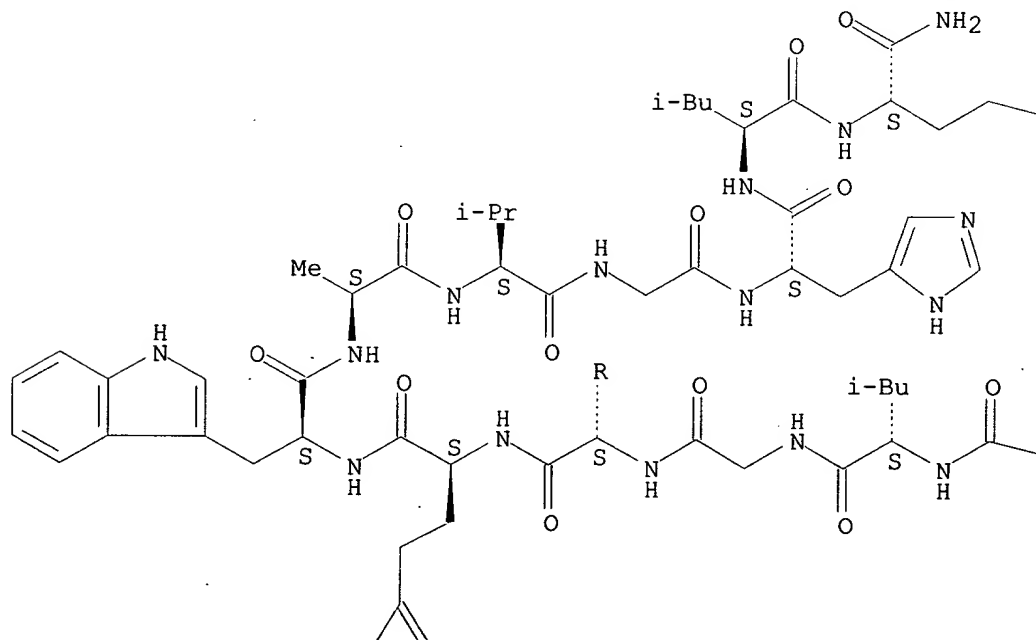
Absolute stereochemistry.



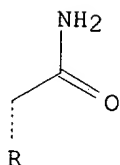
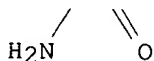
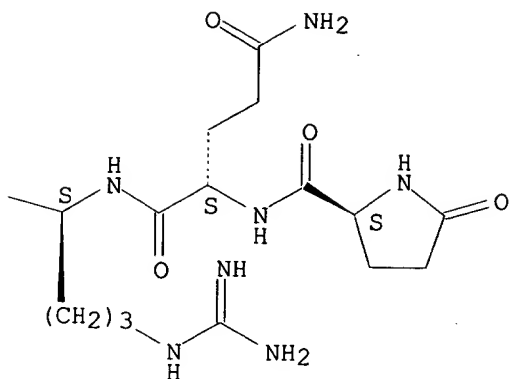
RN 31362-50-2 HCAPLUS  
CN Bombesin (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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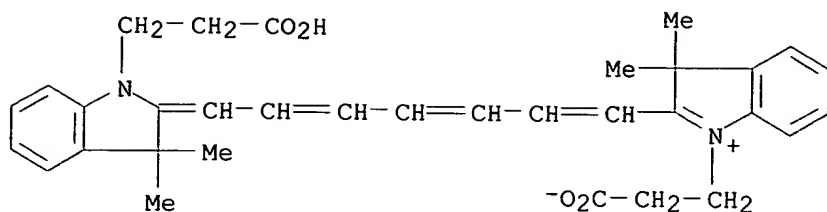
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RN 39379-15-2 HCAPLUS  
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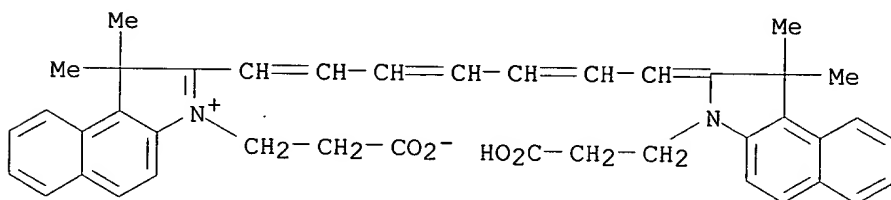
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RN 95837-47-1 HCAPLUS

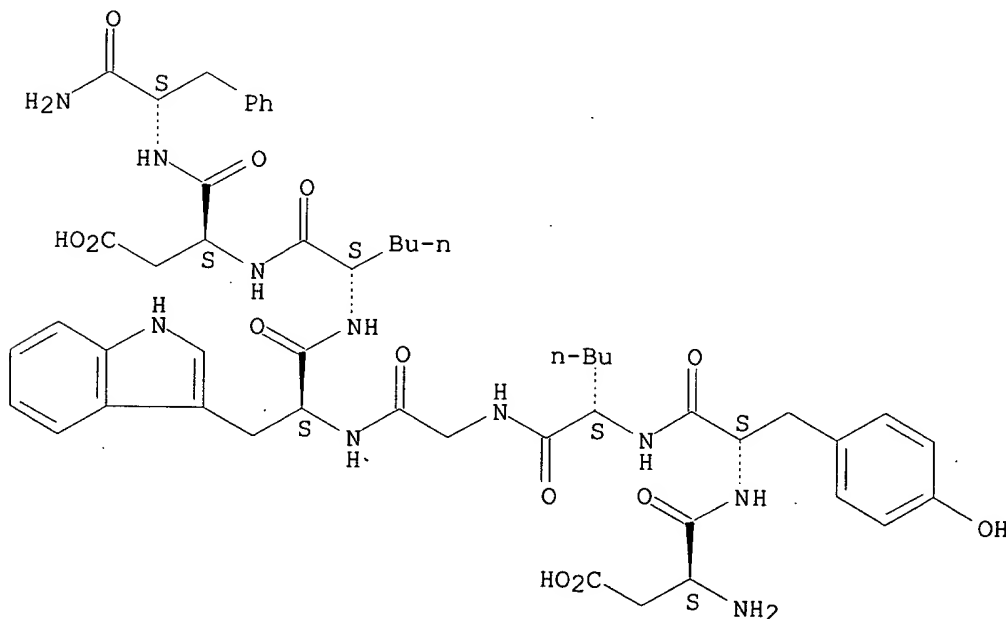
CN 1H-Benz[e]indolium, 3-(2-carboxyethyl)-2-[7-[3-(2-carboxyethyl)-1,3-dihydro-1,1-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-, inner salt (9CI) (CA INDEX NAME)



RN 105466-87-3 HCAPLUS

CN L-Phenylalaninamide, L-.alpha.-aspartyl-L-tyrosyl-L-norleucylglycyl-L-tryptophyl-L-norleucyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

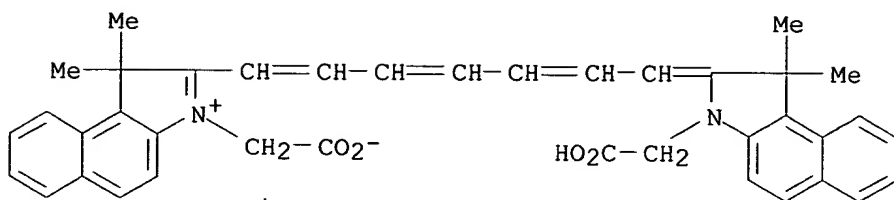
Absolute stereochemistry.



RN 115239-21-9 HCAPLUS

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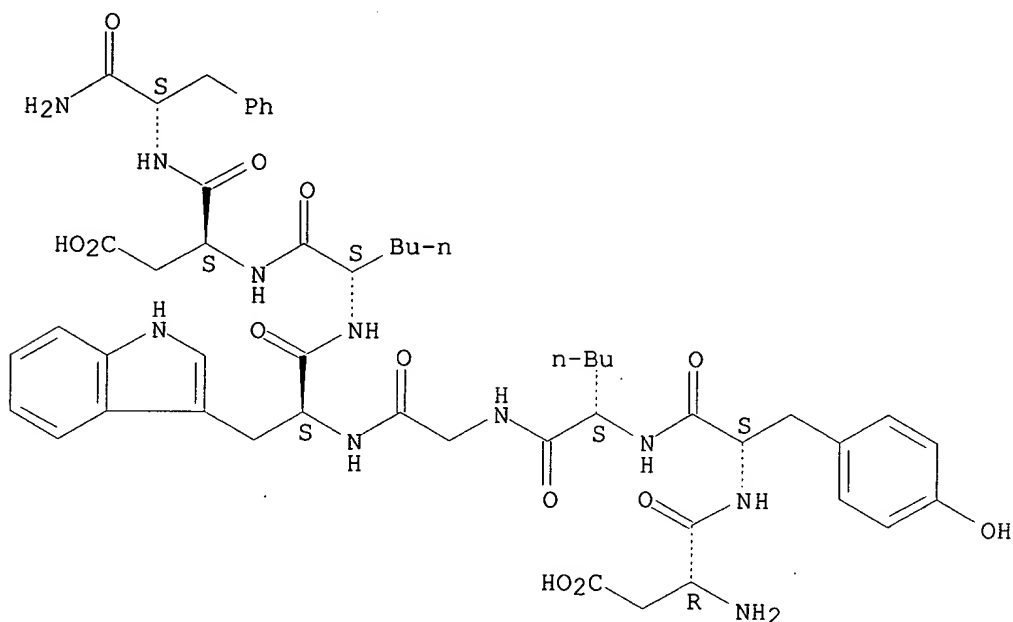




RN 195825-84-4 HCAPLUS

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Absolute stereochemistry.

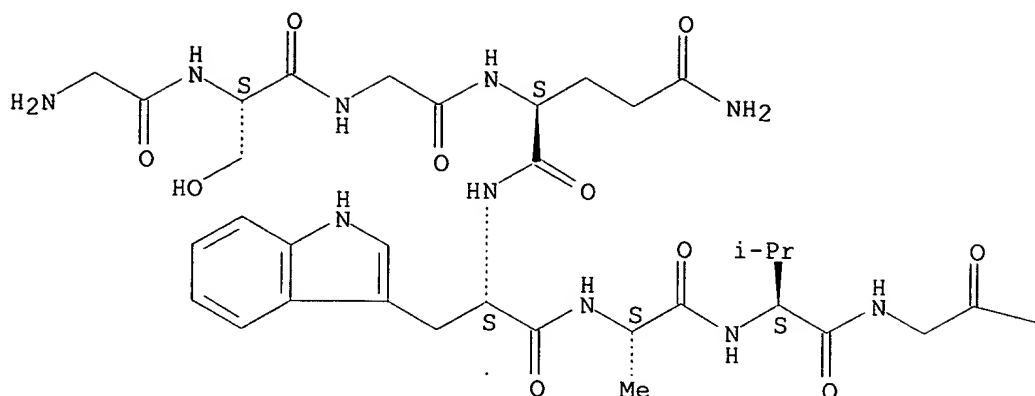


RN 309916-88-9 HCAPLUS

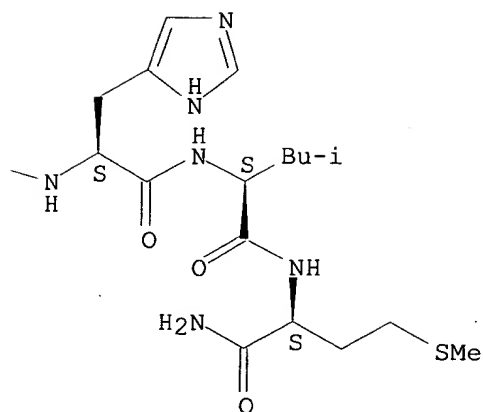
CN L-Methioninamide, glycyl-L-serylglycyl-L-glutaminyll-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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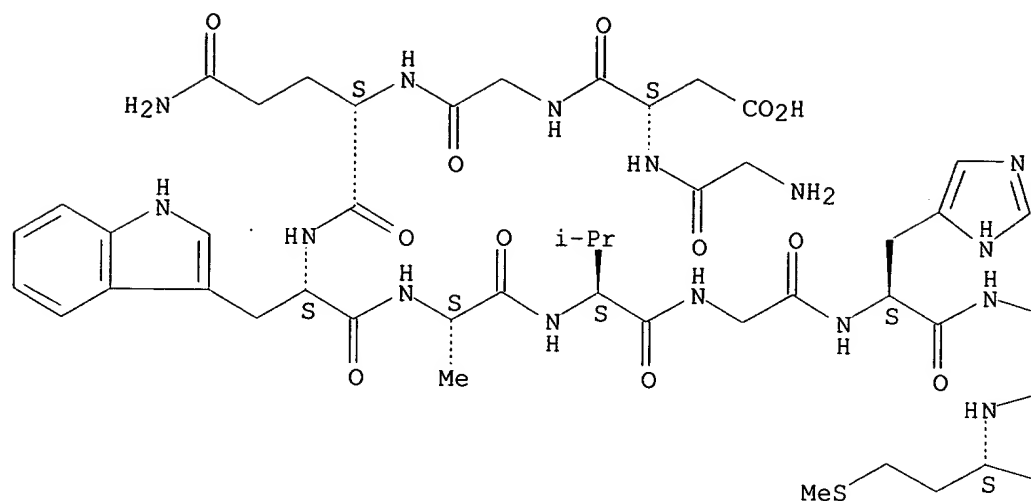
PAGE 1-B



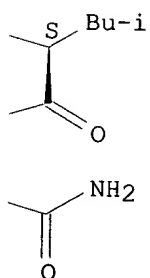
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Absolute stereochemistry.

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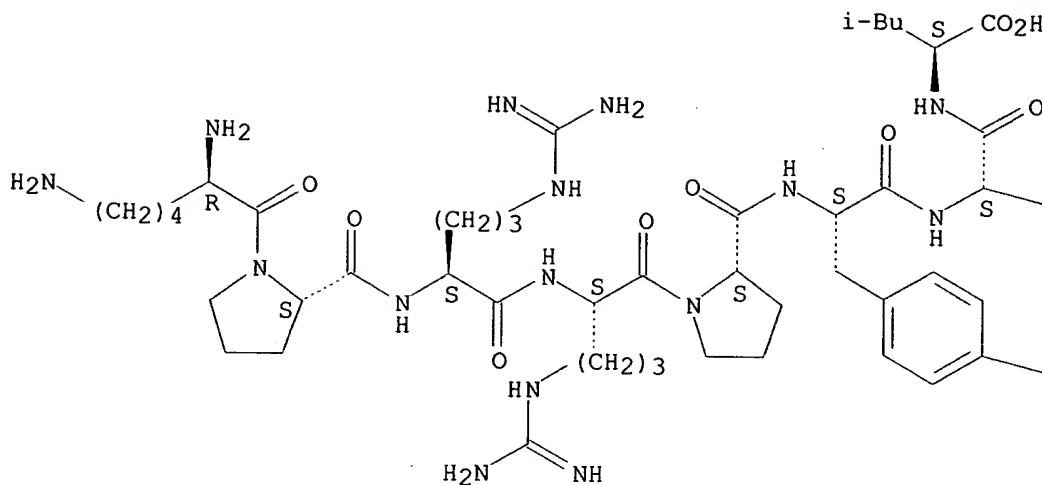
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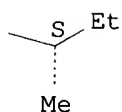
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Absolute stereochemistry.

PAGE 1-A

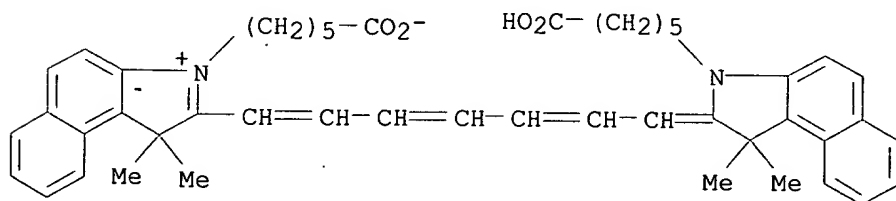


PAGE 1-B



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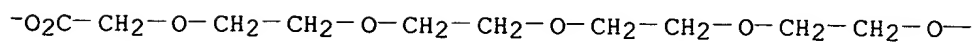
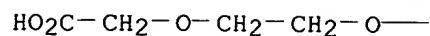
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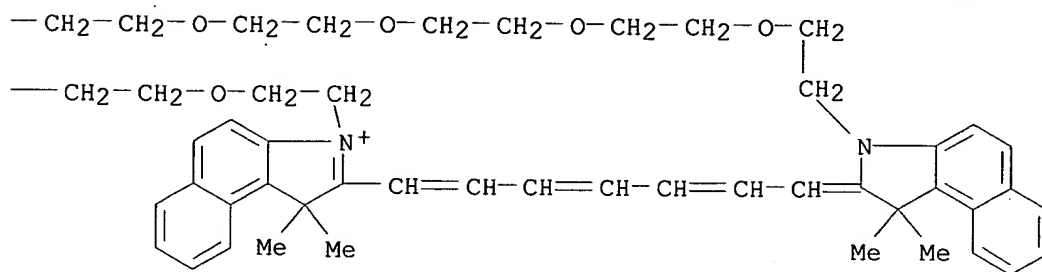
RN 411241-10-6 HCAPLUS

CN INDEX NAME NOT YET ASSIGNED

PAGE 1-A

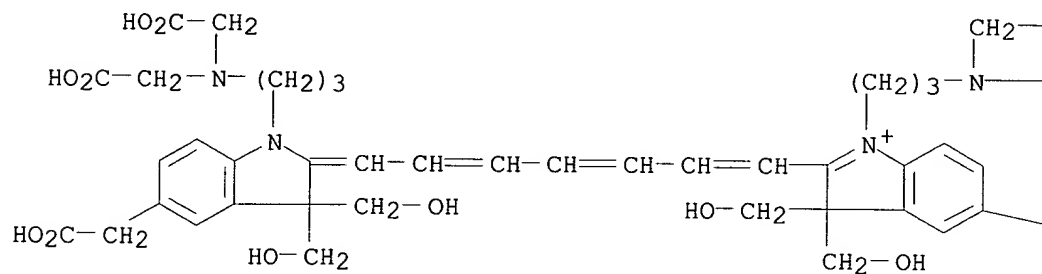


PAGE 1-B

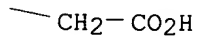
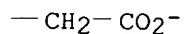
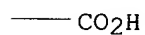


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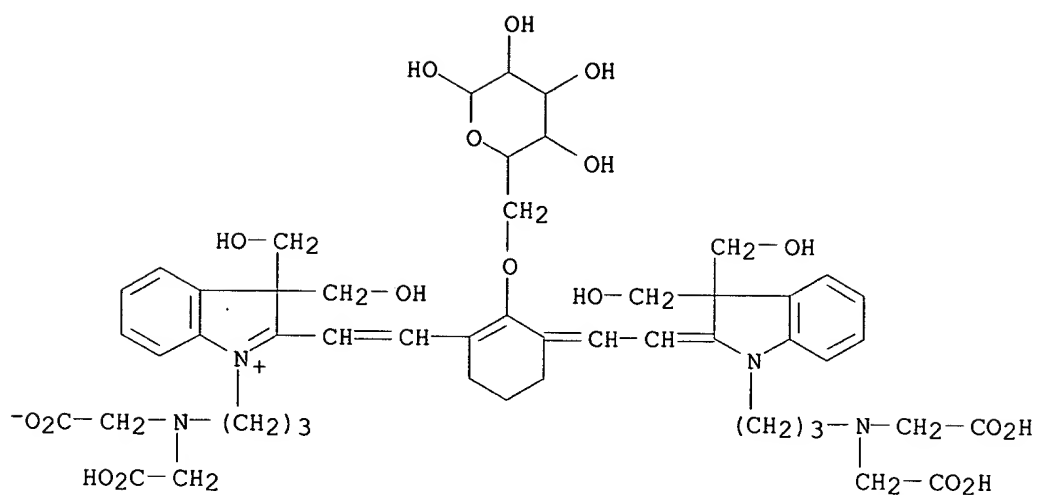
PAGE 1-A



PAGE 1-B



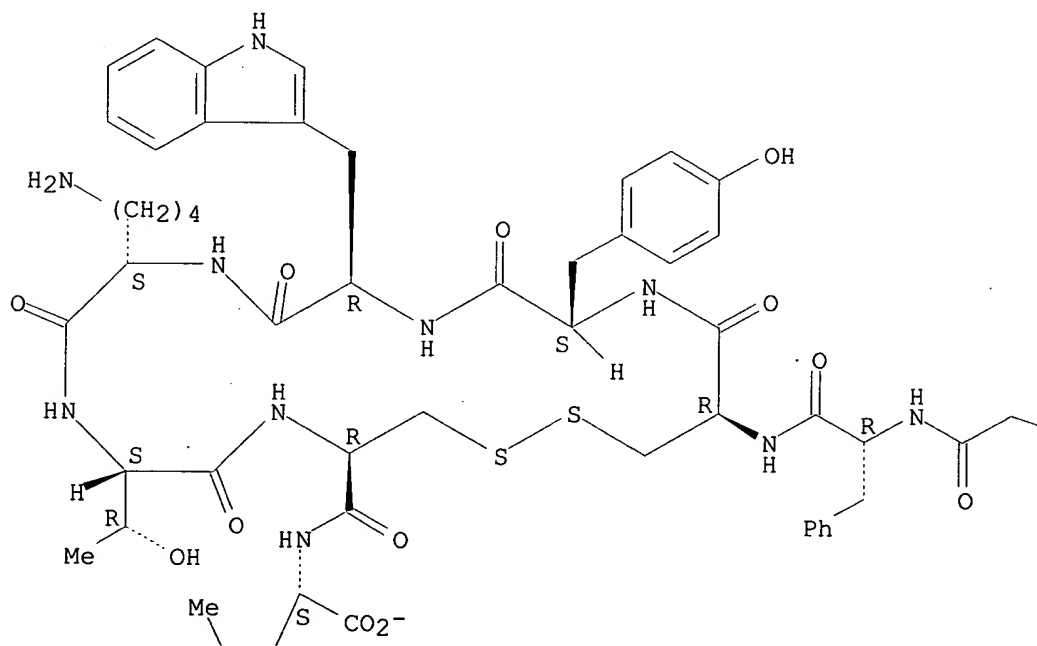
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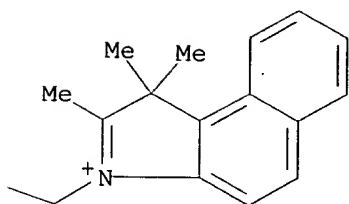
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Absolute stereochemistry.

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PAGE 2-A



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L14 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:677718 HCAPLUS

TITLE: New approach to optical imaging of tumors

AUTHOR(S): Achilefu, Samuel I.; Bugaj, Joseph  
E.; Dorshow, Richard B.; Jimenez, Hermo  
N.; Rajagopalan, Raghavan

CORPORATE SOURCE: Mallinckrodt, Inc., St. Louis, MO, 63134-0840, USA

SOURCE: Proc. SPIE-Int. Soc. Opt. Eng. (2001), 4259(Biomarkers  
and Biological Spectra Imaging), 110-114  
CODEN: PSISDG; ISSN: 0277-786X

PUBLISHER: SPIE-The International Society for Optical Engineering

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Site specific delivery of drugs and contrast agents to tumors protects normal tissues from the cytotoxic effect of drugs, and enhances the contrast between normal and diseased tissues. In optical medicine, biocompatible **dyes** can be used as **phototherapeutics** or as contrast agents. Previous studies have shown that the use of covalent or non-covalent **dye** conjugates of carriers such as antibodies, liposomes, and polysaccharides improves the delivery of such mols. to tumors. However, large biomols. can elicit adverse immunogenic reactions and also result in long blood clearance times, delaying visualization of target tissues. A viable alternative to this strategy is to use small bioactive mol.-**dye** conjugates. These mols. have several advantages over large biomols., including ease of synthesis of a variety of high purity compds. for combinatorial screening of new targets, enhanced diffusivity to solid tumors, and the ability to affect the pharmacokinetics of the conjugates by minor structural changes. Thus, we conjugated a near IR absorbing **dye** to several bioactive peptides that specifically target overexpressed tumor receptors in established rat tumor lines. High tumor uptake of the conjugates was obtained without loss of either the peptide receptor affinity or the **dye** fluorescence. These findings demonstrate the efficacy of a small peptide-**dye** conjugate strategy for in vivo tumor imaging. Site-specific delivery of **photodynamic** therapy agents may also benefit from this approach.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



=&gt; d ibib abs hitstr 3

L14 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:545690 HCAPLUS

DOCUMENT NUMBER: 135:142328

TITLE: Dendrimer precursor indocyanine **dyes** for imagingINVENTOR(S): **Achilefu, Samuel I.; Rajagopalan, Raghavan; Dorshow, Richard B.; Bugaj, Joseph E.**

PATENT ASSIGNEE(S): Mallinckrodt Inc., USA

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053292	A1	20010726	WO 2001-US1407	20010117
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2000-484322 A 20000118

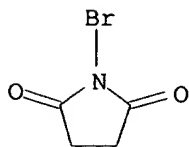
OTHER SOURCE(S): MARPAT 135:142328

AB The sensitivity and specificity of the optical modality can be enhanced by the use of highly absorbing **dyes** as contrast agents. Novel indocyanine **dyes** that absorb and emit light in the near IR region of electromagnetic spectrum are disclosed. These **dyes** are useful for imaging, diagnosis and therapy of various diseased states. Particularly, the mols. of the invention are useful for optical diagnostic imaging and therapy, in endoscopic applications for the detection of tumors and other abnormalities, e.g., atherosclerotic plaques and blood clots, for localized therapy, for **photoacoustic** tumor imaging, detection and therapy, and for sonofluorescence tumor imaging, detection and therapy. The compns. of indocyanine **dyes** are prepd. by conjugating the **dyes** to peptides or biomols. by solid phase synthesis. To prevent in vivo or in vitro fluorescence quenching of the diagnostic or therapeutic compns. of the **dye** mols., 1-50% of DMSO is added. For example, a bis(ethylcarboxymethyl)indocyanine **dye** was prepd. from 1,1,2-trimethyl-[1H]-benz[e]indole and 3-bromopropanoic acid and then the **dye** was conjugated to Octreotate peptide.

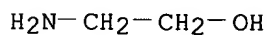
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RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of indocyanine **dyes** for diagnostic or therapeutic compns.)

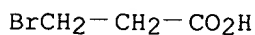
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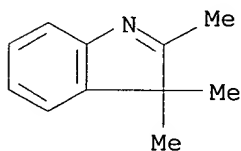
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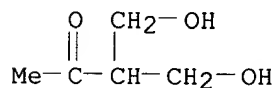
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 CN Propanoic acid, 3-bromo- (9CI) (CA INDEX NAME)



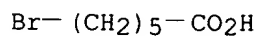
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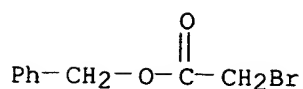
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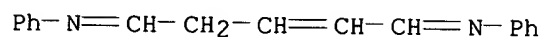
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RN 5437-45-6 HCAPLUS  
 CN Acetic acid, bromo-, phenylmethyl ester (9CI) (CA INDEX NAME)

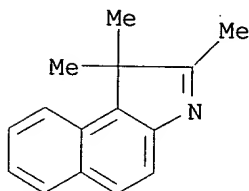


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 CN Benzenamine, N,N'-2-pentene-1,5-diylidenebis-, monohydrochloride (9CI)  
 (CA INDEX NAME)

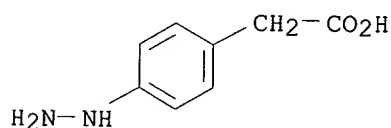


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RN 41532-84-7 HCAPLUS  
 CN 1H-Benz[e]indole, 1,1,2-trimethyl- (9CI) (CA INDEX NAME)

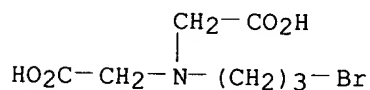


RN 65476-32-6 HCAPLUS  
 CN Benzeneacetic acid, 4-hydrazino-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 309916-92-5 HCAPLUS  
 CN Glycine, N-(3-bromopropyl)-N-(carboxymethyl)- (9CI) (CA INDEX NAME)



IT 25679-24-7P 61010-04-6P 83150-76-9P,  
 Octreotide 95781-56-9P 95837-47-1P  
 105466-87-3P 115239-21-9P 195825-84-4P  
 302794-43-0P 309916-88-9P 309916-89-0P  
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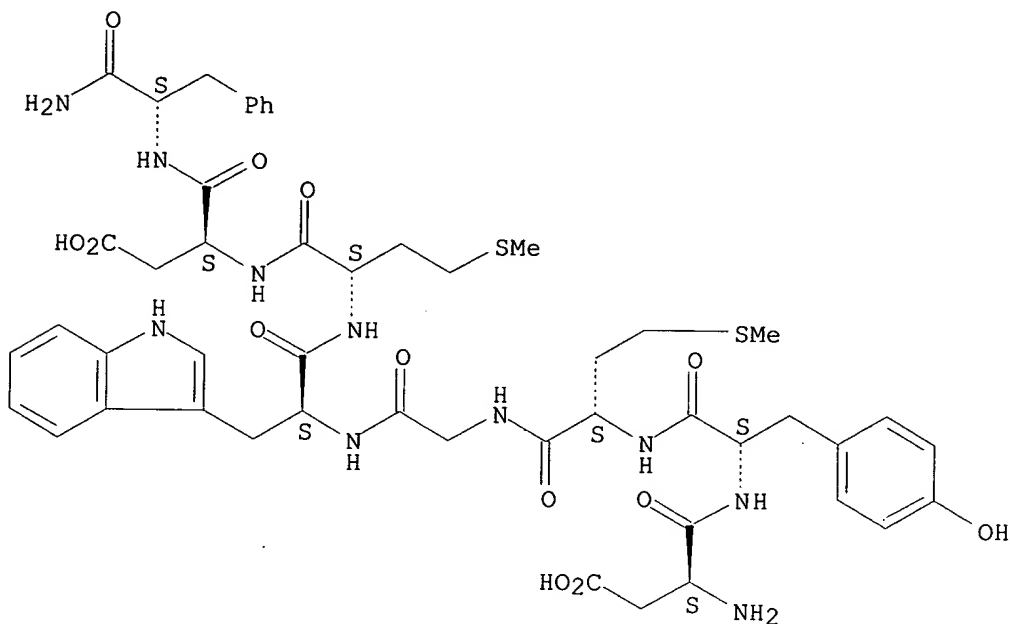
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of indocyanine **dyes** for diagnostic or therapeutic compns.)

RN 25679-24-7 HCAPLUS

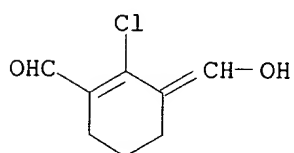
CN Cholecystokinin-8 (swine), 2-desulfo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



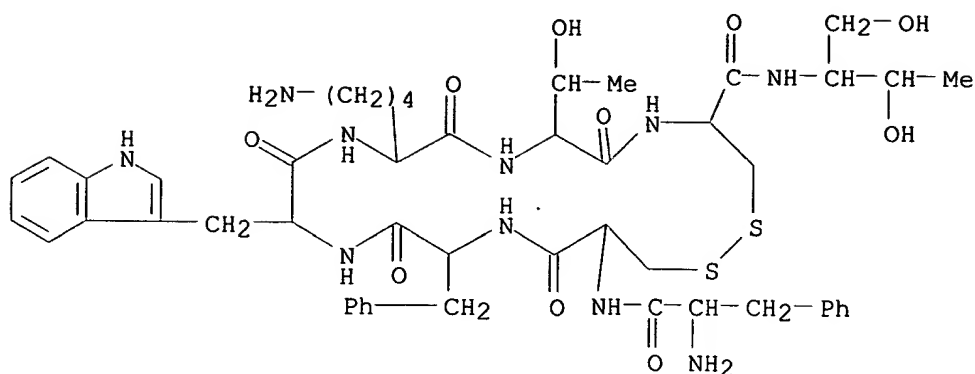
RN 61010-04-6 HCAPLUS

CN 1-Cyclohexene-1-carboxaldehyde, 2-chloro-3-(hydroxymethylene)- (9CI) (CA INDEX NAME)



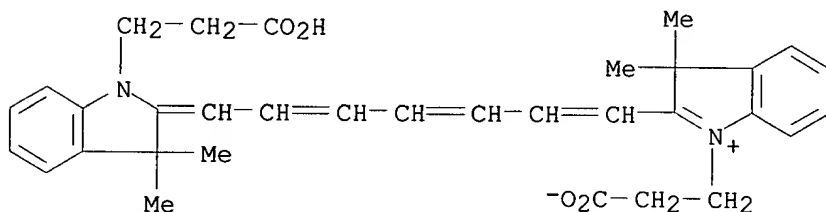
RN 83150-76-9 HCAPLUS

CN L-Cysteinamide, D-phenylalanyl-L-cysteiny-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)



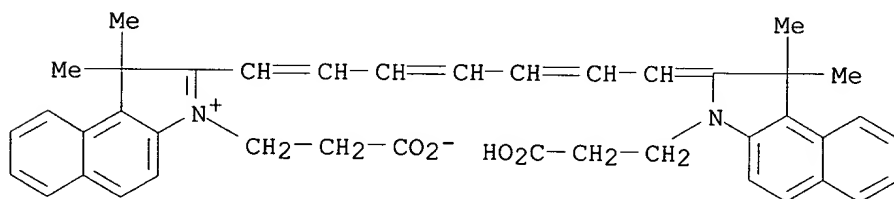
RN 95781-56-9 HCAPLUS

CN 3H-Indolium, 1-(2-carboxyethyl)-2-[7-[1-(2-carboxyethyl)-1,3-dihydro-3,3-dimethyl-2H-indol-2-ylidene]-1,3,5-heptatrienyl]-3,3-dimethyl-, inner salt (9CI) (CA INDEX NAME)



RN 95837-47-1 HCAPLUS

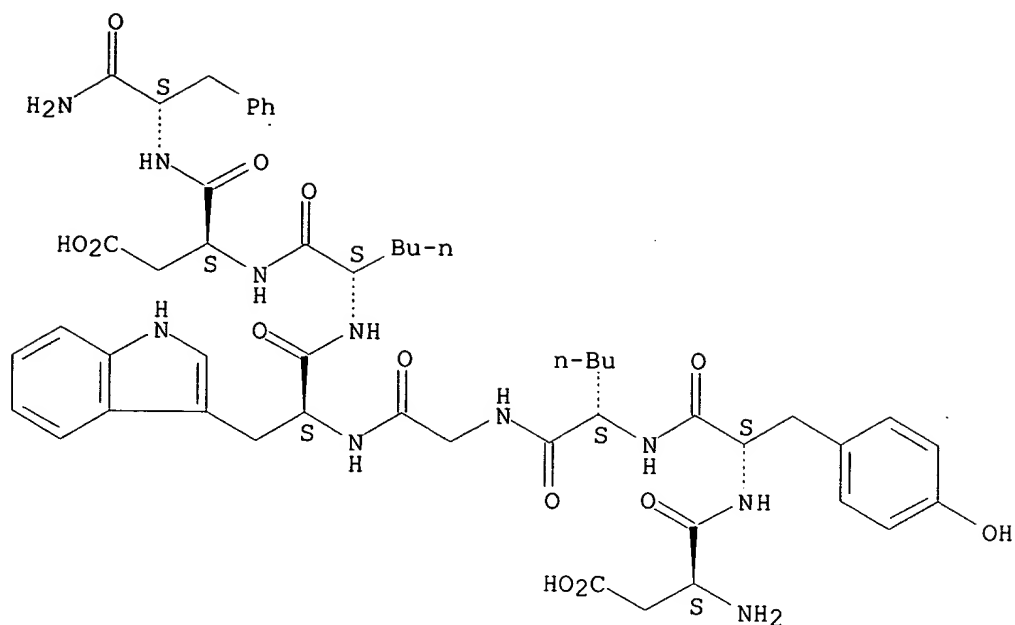
CN 1H-Benz[e]indolium, 3-(2-carboxyethyl)-2-[7-[3-(2-carboxyethyl)-1,3-dihydro-1,1-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-, inner salt (9CI) (CA INDEX NAME)



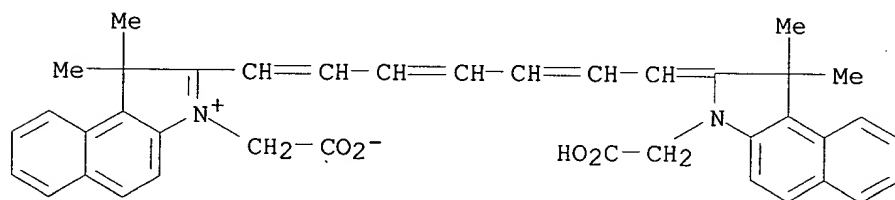
RN 105466-87-3 HCAPLUS

CN L-Phenylalaninamide, L-.alpha.-aspartyl-L-tyrosyl-L-norleucylglycyl-L-tryptophyl-L-norleucyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

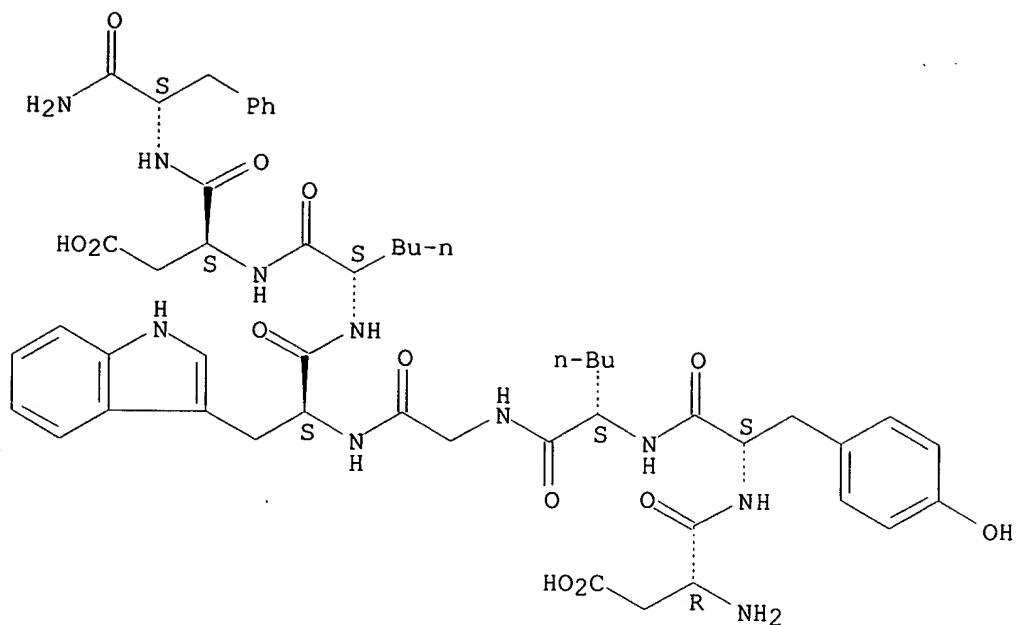


RN 115239-21-9 HCAPLUS  
 CN 1H-Benz[e]indolium, 3-(carboxymethyl)-2-[7-[3-(carboxymethyl)-1,3-dihydro-1,1-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-, inner salt (9CI) (CA INDEX NAME)

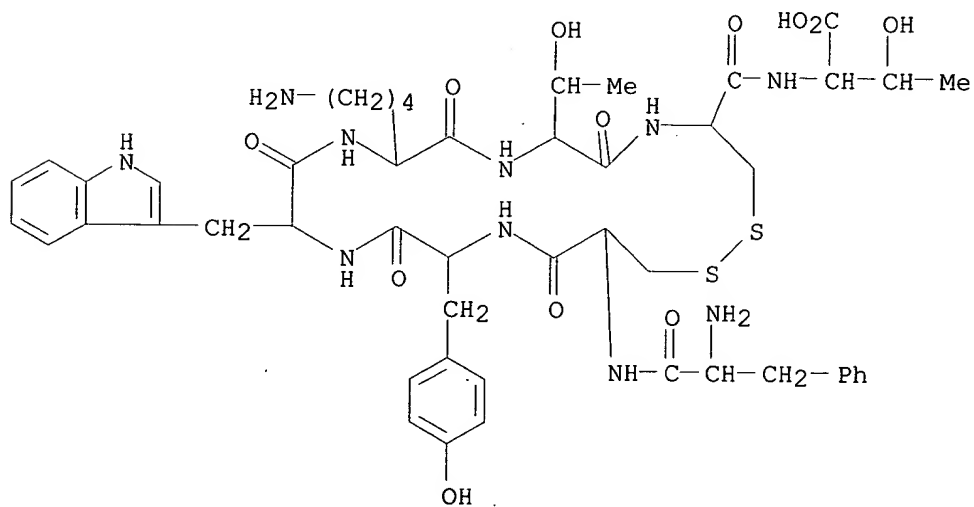


RN 195825-84-4 HCAPLUS  
 CN L-Phenylalaninamide, D-.alpha.-aspartyl-L-tyrosyl-L-norleucylglycyl-L-tryptophyl-L-norleucyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



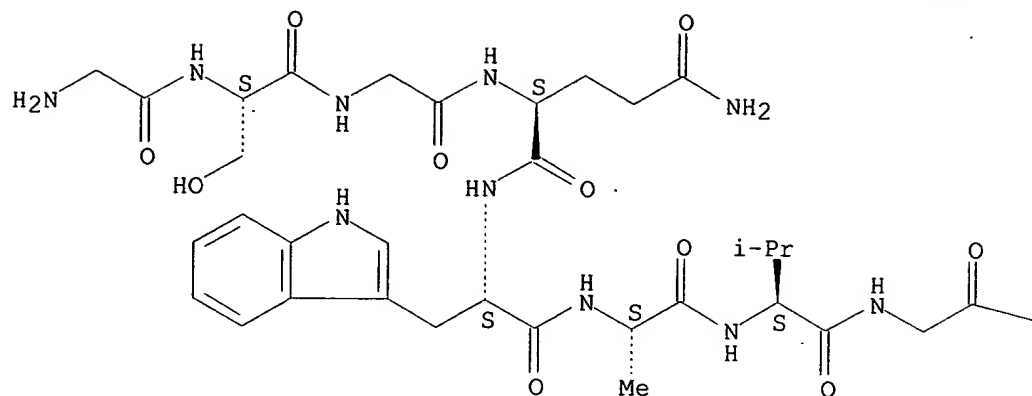
RN 302794-43-0 HCAPLUS  
 CN L-Threonine, D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)



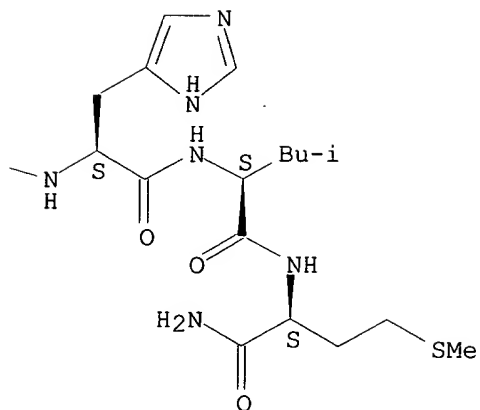
RN 309916-88-9 HCAPLUS  
 CN L-Methioninamide, glycyl-L-serylglycyl-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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PAGE 1-B



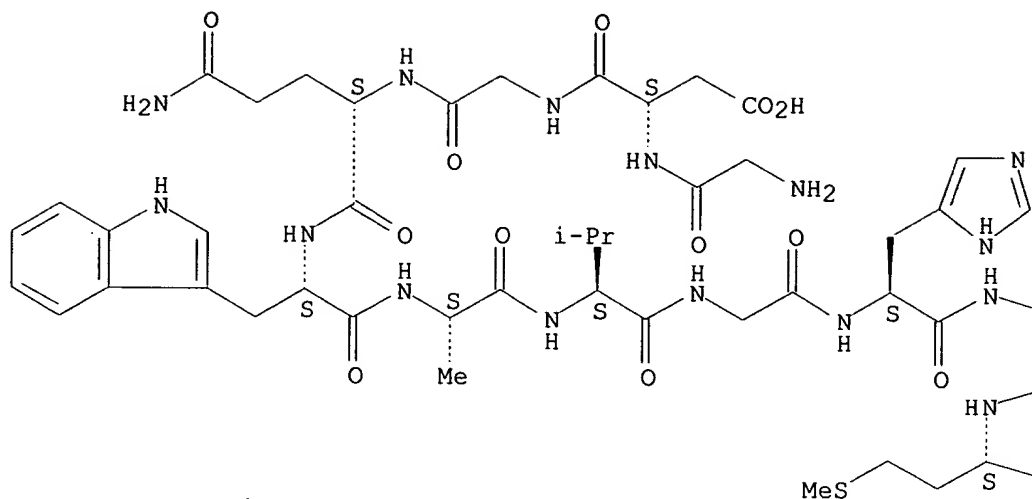
RN 309916-89-0 HCAPLUS

CN L-Methioninamide, glycyl-L-.alpha.-aspartylglycyl-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

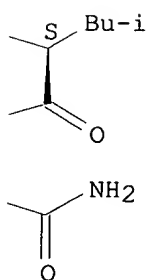
Absolute stereochemistry.



PAGE 1-A



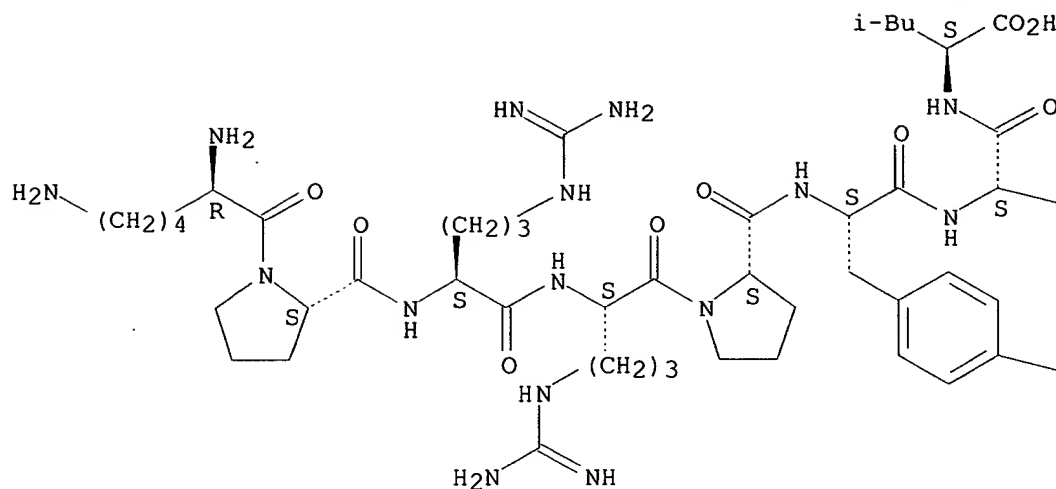
PAGE 1-B



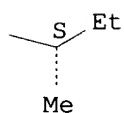
RN 309916-90-3 HCAPLUS  
 CN L-Leucine, D-lysyl-L-prolyl-L-arginyl-L-arginyl-L-prolyl-L-tyrosyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

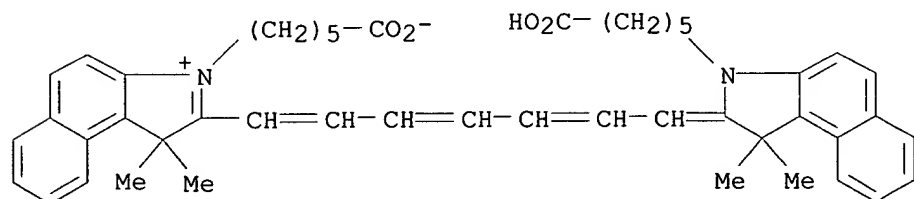


PAGE 1-B



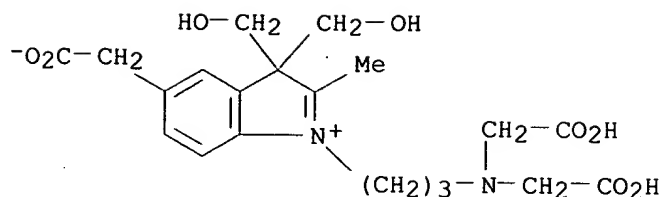
RN 351439-57-1 HCAPLUS

CN 1H-Benz[e]indolium, 3-(5-carboxypentyl)-2-[7-[3-(5-carboxypentyl)-1,3-dihydro-1,1-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-, inner salt (9CI) (CA INDEX NAME)



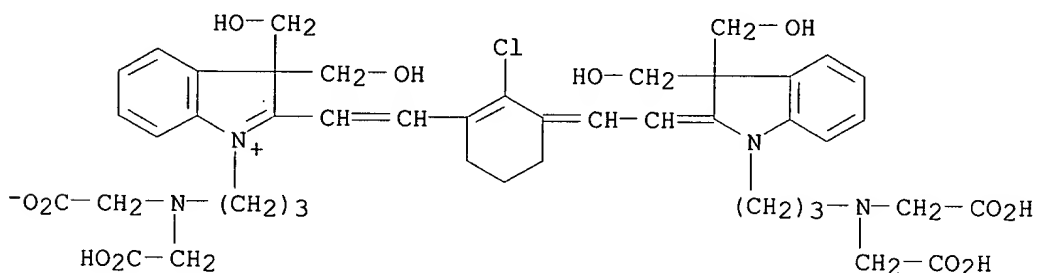
RN 351439-58-2 HCAPLUS

CN 3H-Indolium, 1-[3-[bis(carboxymethyl)amino]propyl]-5-(carboxymethyl)-3,3-bis(hydroxymethyl)-2-methyl-, inner salt (9CI) (CA INDEX NAME)



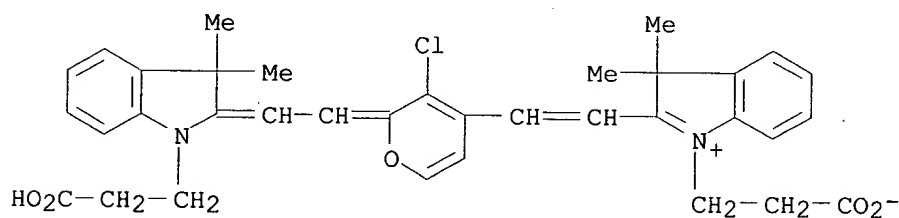
RN 351439-59-3 HCAPLUS

CN 3H-Indolium, 1-[3-[bis(carboxymethyl)amino]propyl]-2-[2-[3-[[1-[3-bis(carboxymethyl)amino]propyl]-1,3-dihydro-3,3-bis(hydroxymethyl)-2H-indol-2-ylidene]ethylidene]-2-chloro-1-cyclohexen-1-yl]ethenyl]-3,3-bis(hydroxymethyl)-, inner salt (9CI) (CA INDEX NAME)



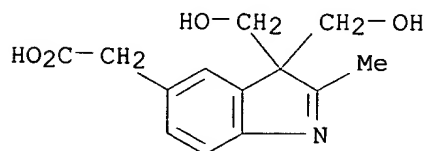
RN 351439-60-6 HCAPLUS

CN 3H-Indolium, 1-(2-carboxyethyl)-2-[2-[2-[[1-(2-carboxyethyl)-1,3-dihydro-3,3-dimethyl-2H-indol-2-ylidene]ethylidene]-3-chloro-2H-pyran-4-yl]ethenyl]-3,3-dimethyl-, inner salt (9CI) (CA INDEX NAME)



RN 351439-68-4 HCAPLUS

CN 3H-Indole-5-acetic acid, 3,3-bis(hydroxymethyl)-2-methyl- (9CI) (CA INDEX NAME)



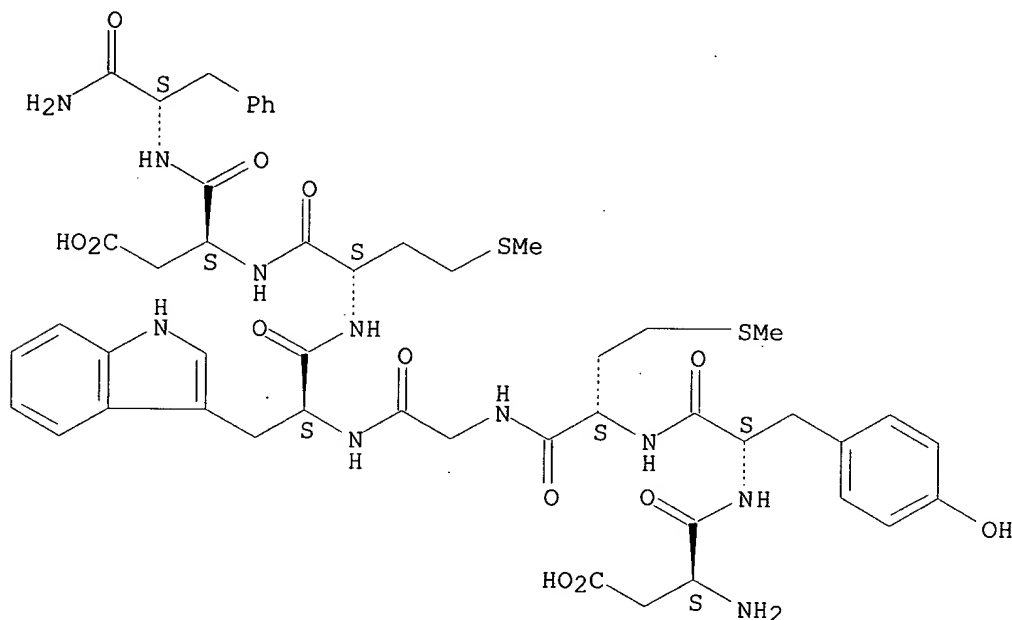
IT 25679-24-7DP, conjugates with indocyanine dyes

83150-76-9DP, Octreotide, conjugates with indocyanine dyes  
 95781-56-9DP, conjugates with peptides 95837-47-1DP,  
 conjugates with peptides 105466-87-3DP, conjugates with  
 indocyanine dyes 115239-21-9DP, conjugates with  
 peptides 195825-84-4DP, conjugates with indocyanine dyes  
 302794-43-0DP, conjugates with indocyanine dyes  
 309916-88-9DP, conjugates with indocyanine dyes  
 309916-89-0DP, conjugates with indocyanine dyes  
 309916-90-3DP, conjugates with indocyanine dyes  
 351439-57-1DP, conjugates with peptides 351439-58-2DP,  
 conjugates with peptides 351439-59-3DP, conjugates with peptides  
 351439-60-6DP, conjugates with peptides  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)  
 (prepn. of indocyanine dyes for diagnostic or therapeutic  
 compns.)

RN 25679-24-7 HCAPLUS

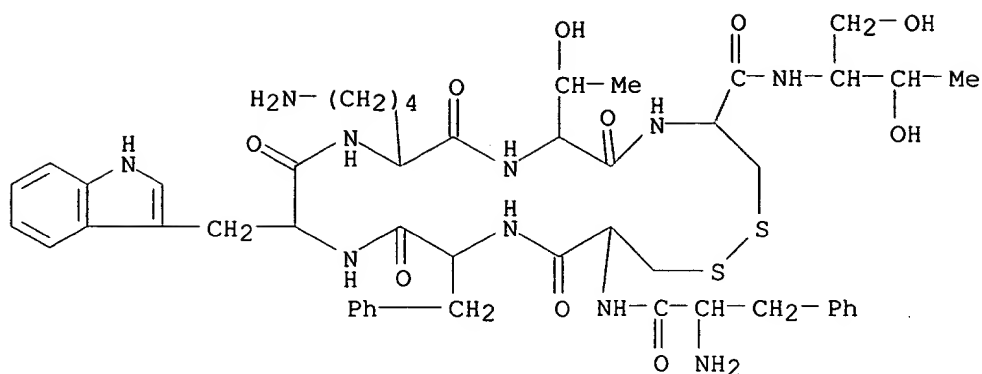
CN Cholecystokinin-8 (swine), 2-desulfo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



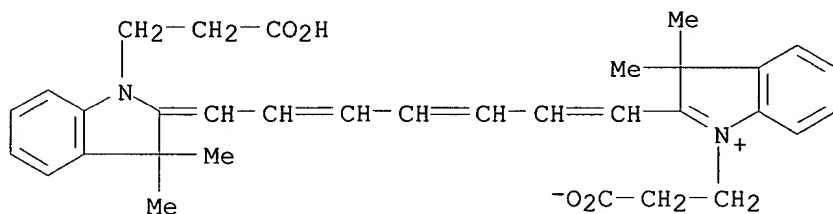
RN 83150-76-9 HCAPLUS

CN L-Cysteinamide, D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME).



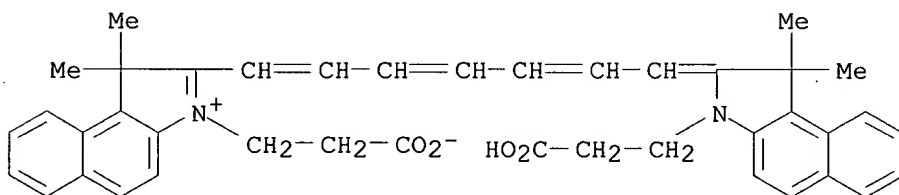
RN 95781-56-9 HCAPLUS

CN 3H-Indolium, 1-(2-carboxyethyl)-2-[7-[1-(2-carboxyethyl)-1,3-dihydro-3,3-dimethyl-2H-indol-2-ylidene]-1,3,5-heptatrienyl]-3,3-dimethyl-, inner salt (9CI) (CA INDEX NAME)



RN 95837-47-1 HCAPLUS

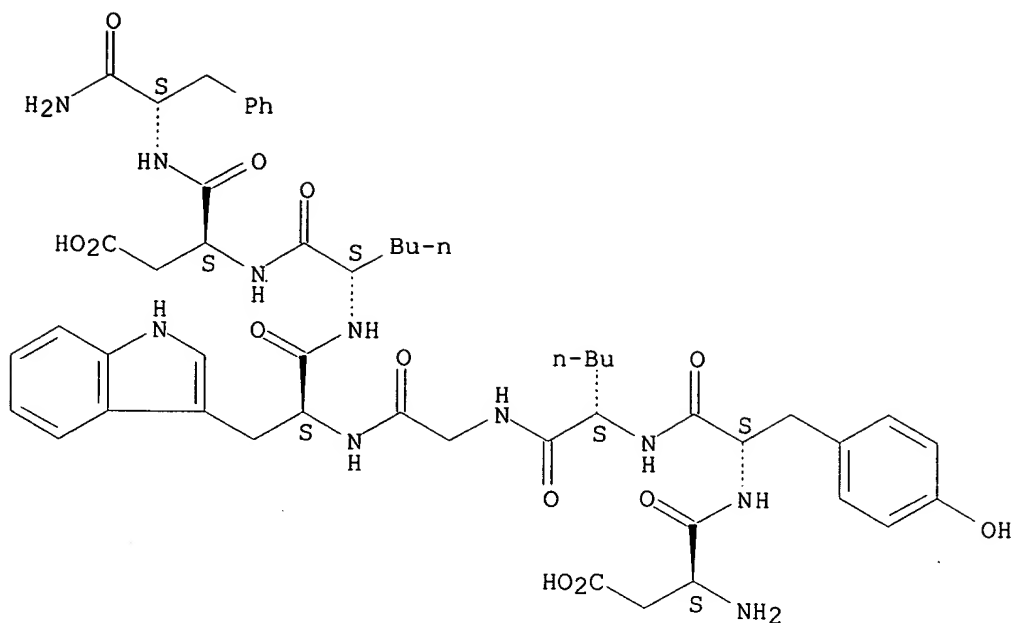
CN 1H-Benz[e]indolium, 3-(2-carboxyethyl)-2-[7-[3-(2-carboxyethyl)-1,3-dihydro-1,1-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-, inner salt (9CI) (CA INDEX NAME)



RN 105466-87-3 HCAPLUS

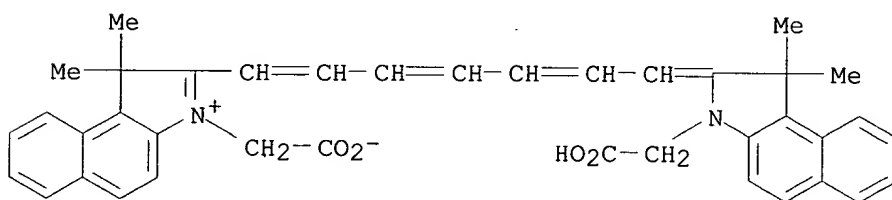
CN L-Phenylalaninamide, L-.alpha.-aspartyl-L-tyrosyl-L-norleucylglycyl-L-tryptophyl-L-norleucyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 115239-21-9 HCAPLUS

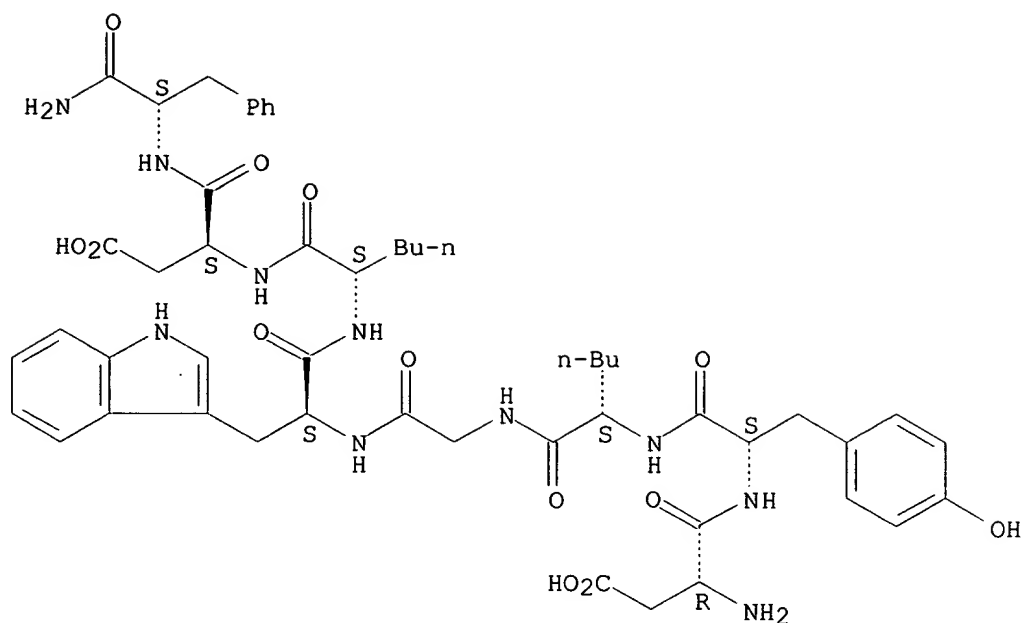
CN 1H-Benz[e]indolium, 3-(carboxymethyl)-2-[7-[3-(carboxymethyl)-1,3-dihydro-1,1-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-, inner salt (9CI) (CA INDEX NAME)



RN 195825-84-4 HCAPLUS

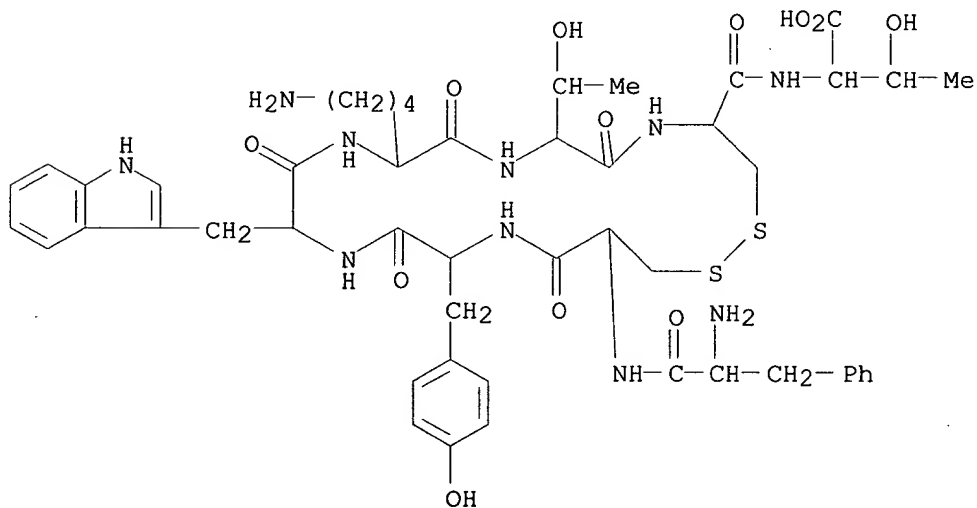
CN L-Phenylalaninamide, D-.alpha.-aspartyl-L-tyrosyl-L-norleucylglycyl-L-tryptophyl-L-norleucyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 302794-43-0 HCAPLUS

CN L-Threonine, D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)

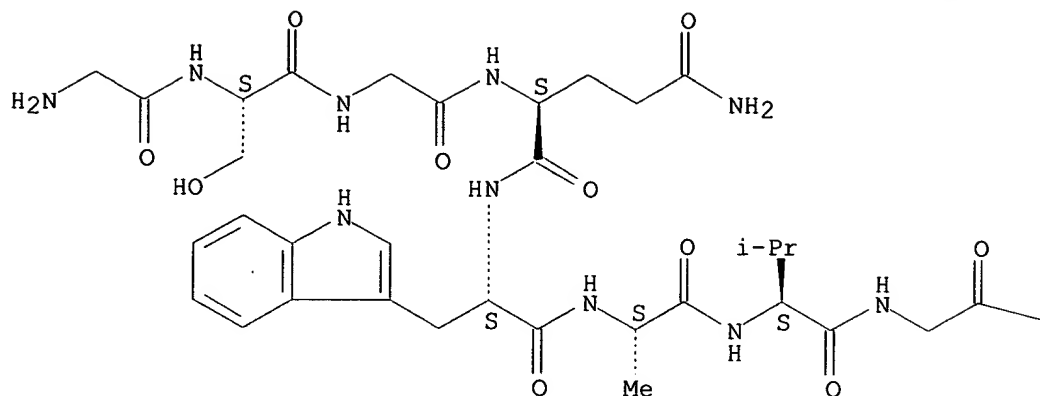


RN 309916-88-9 HCAPLUS

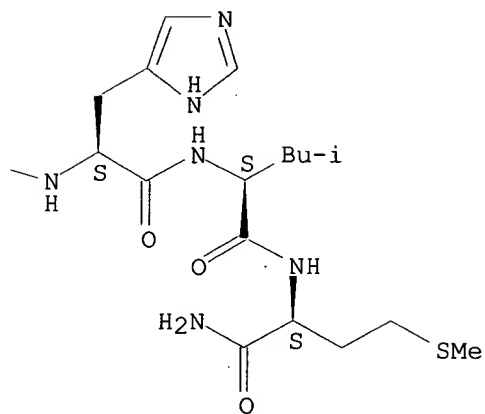
CN L-Methioninamide, glycyl-L-serylglycyl-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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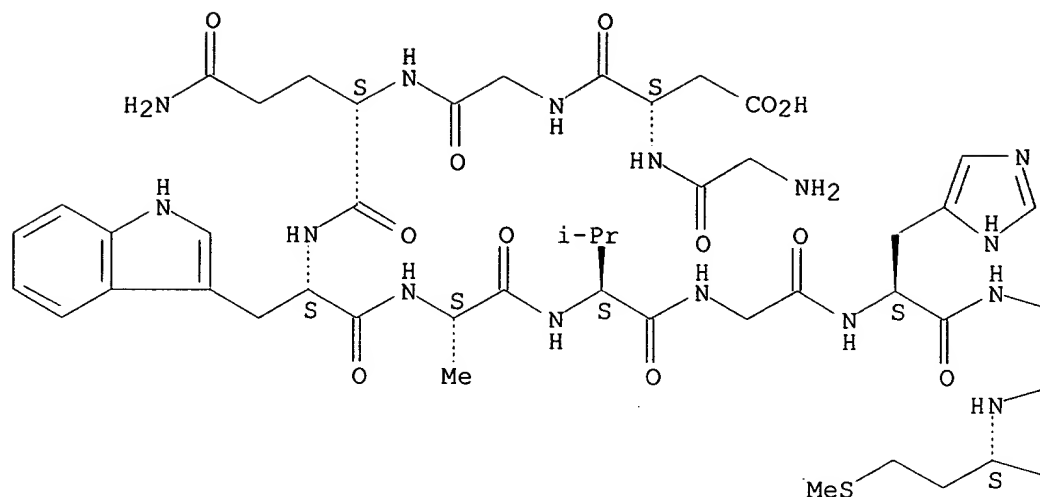


RN 309916-89-0 HCAPLUS  
 CN L-Methioninamide, glycyl-L-.alpha.-aspartylglycyl-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

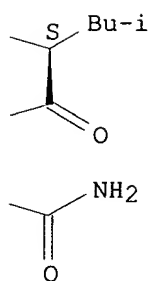
Absolute stereochemistry.



PAGE 1-A



PAGE 1-B

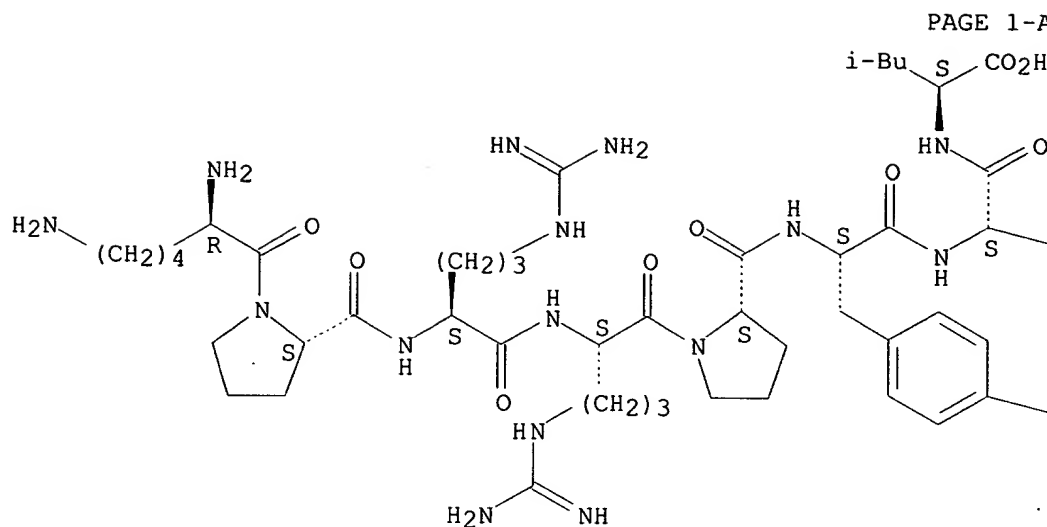


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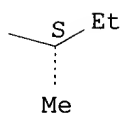
CN L-Leucine, D-lysyl-L-prolyl-L-arginyl-L-arginyl-L-prolyl-L-tyrosyl-L-isoleucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

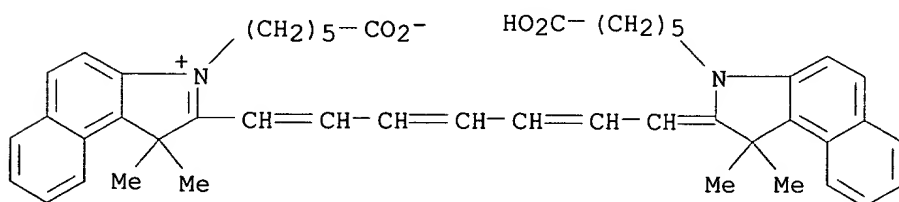


PAGE 1-B



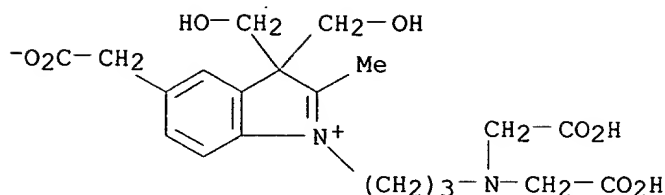
RN 351439-57-1 HCAPLUS

CN 1H-Benz[e]indolium, 3-(5-carboxypentyl)-2-[7-[3-(5-carboxypentyl)-1,3-dihydro-1,1-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-, inner salt (9CI) (CA INDEX NAME)



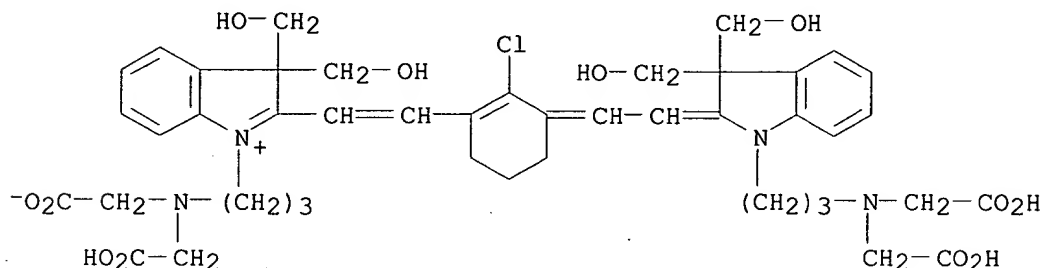
RN 351439-58-2 HCAPLUS

CN 3H-Indolium, 1-[3-[bis(carboxymethyl)amino]propyl]-5-(carboxymethyl)-3,3-bis(hydroxymethyl)-2-methyl-, inner salt (9CI) (CA INDEX NAME)



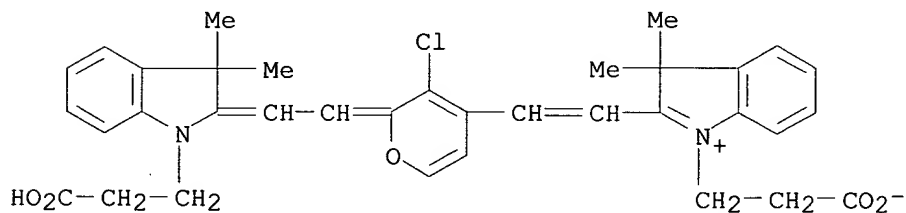
RN 351439-59-3 HCAPLUS

CN 3H-Indolium, 1-[3-[bis(carboxymethyl)amino]propyl]-2-[2-[3-[[1-[3-bis(carboxymethyl)amino]propyl]-1,3-dihydro-3,3-bis(hydroxymethyl)-2H-indol-2-ylidene]ethylidene]-2-chloro-1-cyclohexen-1-yl]ethenyl]-3,3-bis(hydroxymethyl)-, inner salt (9CI) (CA INDEX NAME)



RN 351439-60-6 HCAPLUS

CN 3H-Indolium, 1-(2-carboxyethyl)-2-[2-[2-[[1-(2-carboxyethyl)-1,3-dihydro-3,3-dimethyl-2H-indol-2-ylidene]ethylidene]-3-chloro-2H-pyran-4-yl]ethenyl]-3,3-dimethyl-, inner salt (9CI) (CA INDEX NAME)

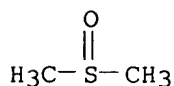


IT 67-68-5, Dimethyl sulfoxide, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(prepn. of indocyanine **dyes** for diagnostic or therapeutic  
comps.)

RN 67-68-5 HCAPLUS

CN Methane, sulfinylbis- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

CEPERLEY 09/898,885

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

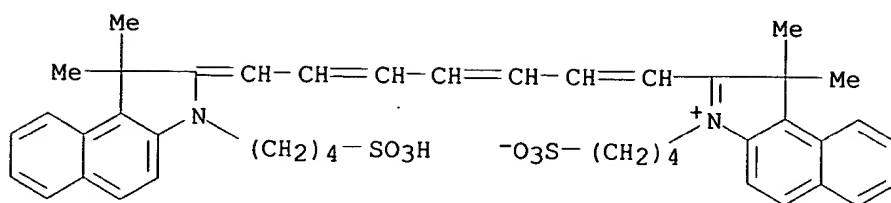
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L14 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:434263 HCAPLUS  
 DOCUMENT NUMBER: 136:196239  
 TITLE: Site-specific tumor-targeted fluorescent contrast agents  
 AUTHOR(S): Achilefu, Samuel I.; Bugaj, Joseph E.; Dorshow, Richard B.; Jimenez, Hermon N.; Rajagopalan, Raghavan; Wilhelm, R. Randy; Webb, Elizabeth G.; Erion, Jack L.  
 CORPORATE SOURCE: Mallinckrodt, Inc., St. Louis, MO, 63042, USA  
 SOURCE: Proceedings of SPIE-The International Society for Optical Engineering (2001), 4156(Clinical Lasers and Diagnostics), 69-78  
 CODEN: PSISDG; ISSN: 0277-786X  
 PUBLISHER: SPIE-The International Society for Optical Engineering  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Site-specific delivery of drugs and contrast agents to tumors protects normal tissues from the cytotoxic effect of drugs, and enhances the contrast between normal and diseased tissues. In optical medicine, biocompatible **dyes** can be used as **photo** therapeutics or as contrast agents. Previous studies have shown that the use of covalent or non-covalent **dye** conjugates of carriers such as antibodies, liposomes, and polysaccharides improves the delivery of such mols. to tumors. However, large biomols. can elicit adverse immunogenic reactions and also result in prolonged blood circulation times, delaying visualization of target tissues. A viable alternative to this strategy is to use small bioactive mol.-**dye** conjugates. These mols. have several advantages over large biomols., including ease of synthesis of a variety of high purity compds. for combinatorial screening of new targets, enhanced diffusivity to solid tumors, and the ability to affect the pharmacokinetics of the conjugates by minor structural changes. Thus, we conjugated a near IR light absorbing **dye** to bioactive peptides that specifically target over expressed tumor receptors in established rat tumor lines. High tumor uptake of the conjugates was obtained without loss of either the peptide receptor affinity or the **dye** fluorescence. These findings demonstrate the efficacy of a small peptide-**dye** conjugate strategy for in vivo tumor imaging. Site-specific delivery of **photodynamic** therapy agents may also benefit from this approach.

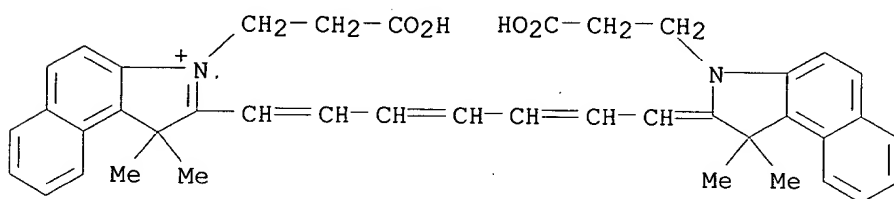
IT 3599-32-4, Indocyanine green  
 RL: DGN (Diagnostic use); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
 (site-specific tumor-targeted fluorescent contrast agents)

RN 3599-32-4 HCAPLUS  
 CN 1H-Benz[e]indolium, 2-[7-[1,3-dihydro-1,1-dimethyl-3-(4-sulfobutyl)-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-3-(4-sulfobutyl)-, inner salt, sodium salt (9CI) (CA INDEX NAME)



● Na

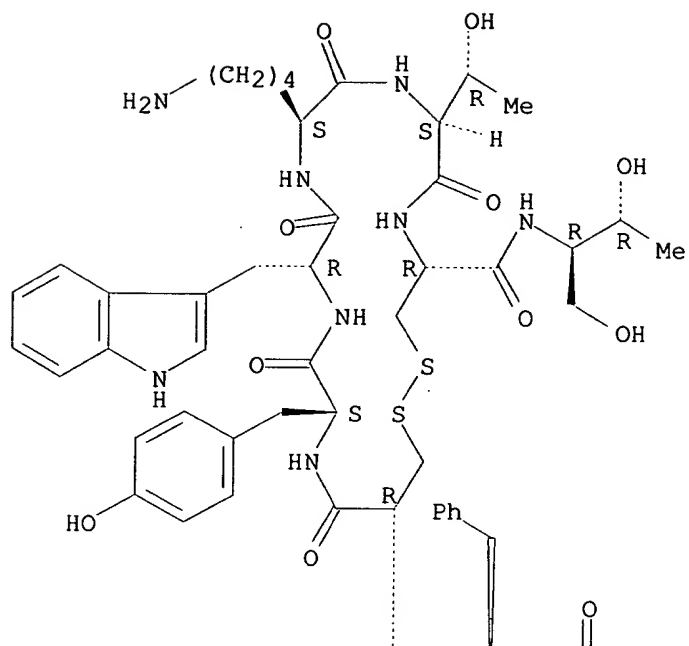
IT **317809-26-0P**, Cypate  
 RL: DGN (Diagnostic use); RCT (Reactant); SPN (Synthetic preparation);  
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);  
 USES (Uses)  
 (site-specific tumor-targeted fluorescent contrast agents)  
 RN 317809-26-0 HCAPLUS  
 CN 1H-Benz[e]indolium, 3-(2-carboxyethyl)-2-[7-[3-(2-carboxyethyl)-1,3-dihydro-1,1-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-, bromide (9CI) (CA INDEX NAME)

● Br<sup>-</sup>

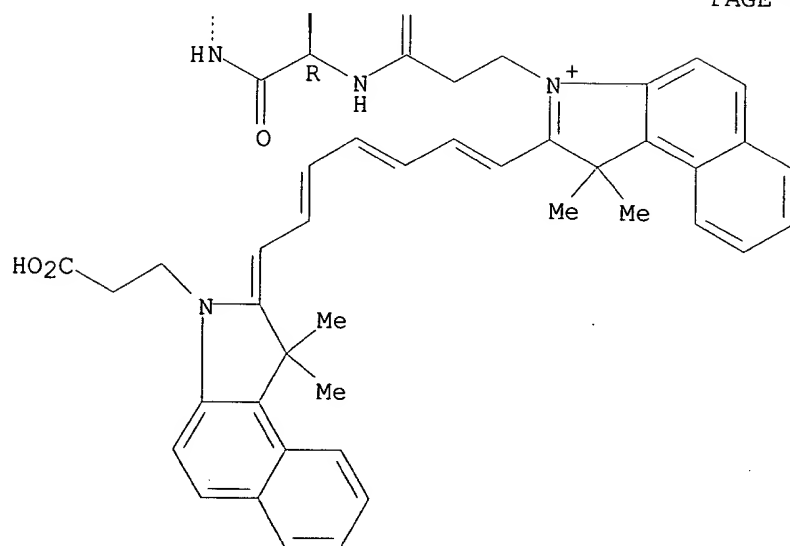
IT **317809-27-1P**, Cytate **401819-24-7P**  
 RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (site-specific tumor-targeted fluorescent contrast agents)  
 RN 317809-27-1 HCAPLUS  
 CN L-Cysteinamide, N-[3-[2-[7-[3-(2-carboxyethyl)-1,3-dihydro-1,1-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-1,1-dimethyl-1H-benz[e]indolium-3-yl]-1-oxopropyl]-D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]-, bromide, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.

PAGE 1-A



PAGE 2-A



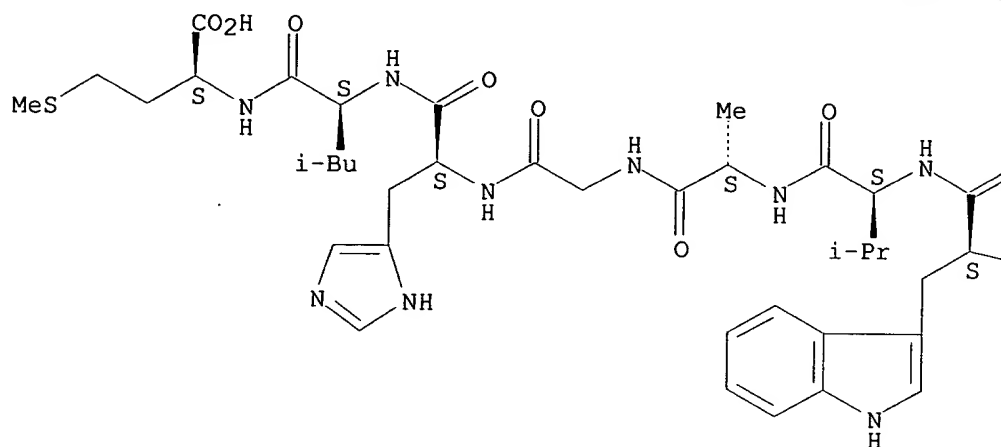
PAGE 3-A

 $\text{Br}^-$

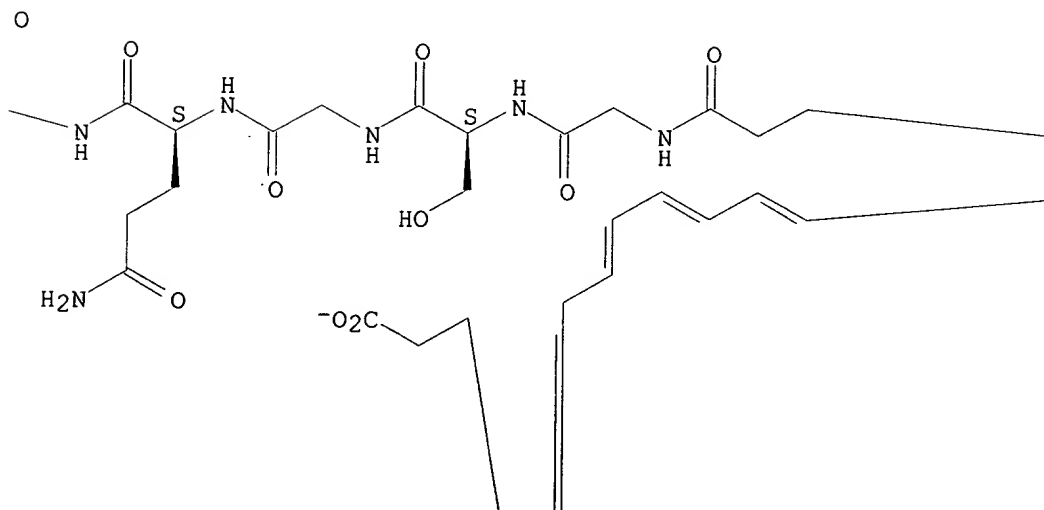
RN 401819-24-7 HCAPLUS  
 CN L-Methionine, N-[3-[2-[7-[1-(2-carboxyethyl)-1,3-dihydro-3,3-dimethyl-2H-benz[e]indol-2-ylidene]-1,3,5-heptatrienyl]-3,3-dimethyl-3H-benz[e]indolium-1-yl]-1-oxopropyl]glycyl-L-serylglycyl-L-glutaminy-L-tryptophyl-L-valyl-L-alanylglycyl-L-histidyl-L-leucyl-, inner salt (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.

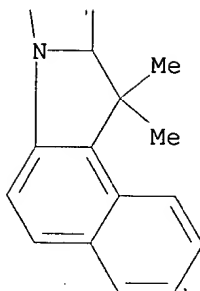
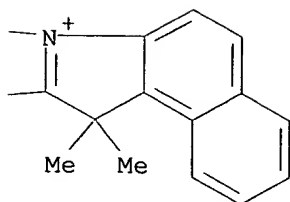
PAGE 1-A



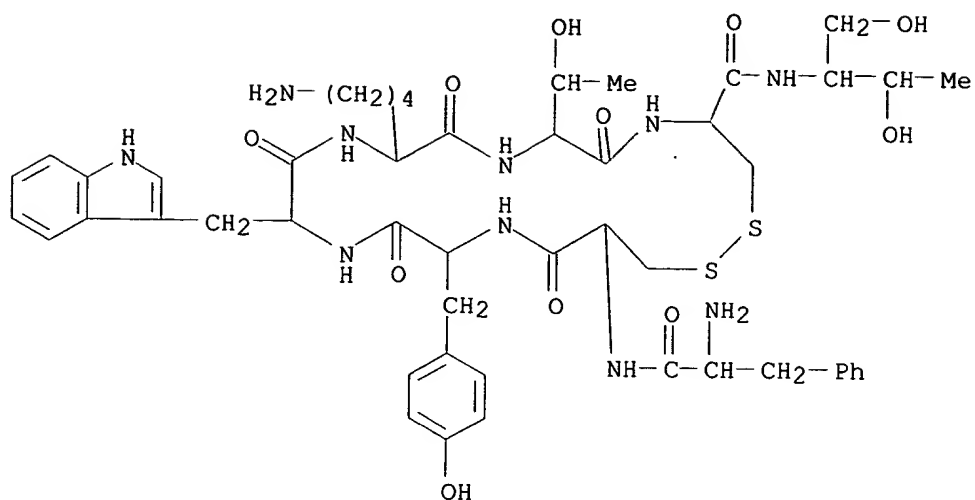
PAGE 1-B







IT **103667-46-5 401819-25-8**  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (site-specific tumor-targeted fluorescent contrast agents)  
 RN 103667-46-5 HCAPLUS  
 CN L-Cysteinamide, D-phenylalanyl-L-cysteiny-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic  
 (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)

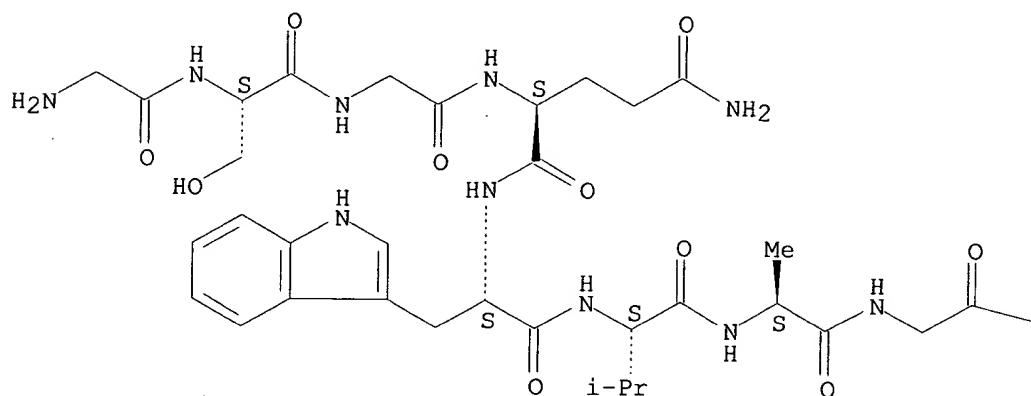


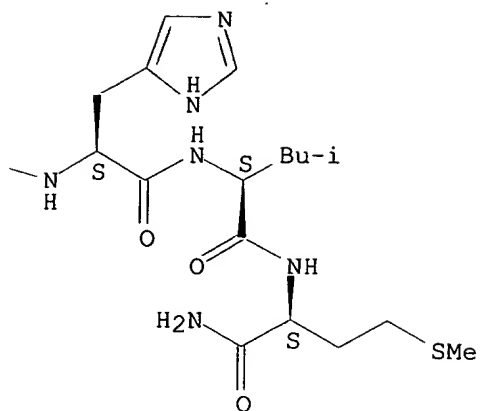
RN 401819-25-8 HCAPLUS

CN L-Methioninamide, glycyl-L-serylglycyl-L-glutaminyl-L-tryptophyl-L-valyl-L-alanylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT:

28

THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=&gt; d ibib abs hitstr 5

L14 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:842014 HCAPLUS

DOCUMENT NUMBER: 134:21520

TITLE: Novel cyanine and indocyanine **dye**  
bioconjugates for biomedical applicationsINVENTOR(S): **Achilefu, Samuel; Dorshow, Richard  
Bradley; Bugaj, Joseph Edward;  
Rajagopalan, Raghavan**

PATENT ASSIGNEE(S): Mallinckrodt Inc., USA

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000071162	A2	20001130	WO 2000-US11060	20000426
WO 2000071162	A3	20010705		
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6217848	B1	20010417	US 1999-325769	19990604
EP 1178830	A2	20020213	EP 2000-926343	20000426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:				
	US 1999-135060P	P	19990520	
	US 1999-325769	A	19990604	
	WO 2000-US11060	W	20000426	

OTHER SOURCE(S): MARPAT 134:21520

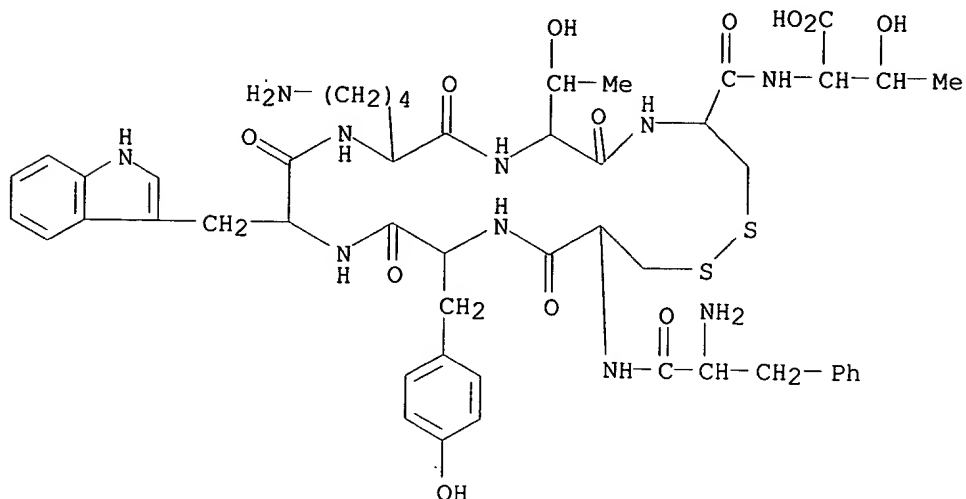
AB **Dye**-peptide conjugates useful for diagnostic imaging and therapy are disclosed. The **dye**-peptide conjugates include several cyanine **dyes** with a variety of bis- and tetrakis(carboxylic acid) homologs. The small size of the compds. allows more favorable delivery to tumor cells as compared to larger mol. wt. imaging agents. The various **dyes** are useful over the range of 350-1300 nm, the exact range being dependent upon the particular **dye**. Use of dimethylsulfoxide helps to maintain the fluorescence of the compds. The mols. of the invention are useful for diagnostic imaging and therapy, in endoscopic applications for the detection of tumors and other abnormalities and for localized therapy, for **photoacoustic** tumor imaging, detection and therapy, and for sonofluorescence tumor imaging, detection and therapy. For example, monooctreotate-bisethylcarboxymethyl indocyanine **dye** (Cytate 1) was prepd. (yield of 80%) and evaluated in the CA20948 Lewis rat model of pancreatic acinar carcinoma. Using the CCD camera, strong localization of this **dye** was obsd. in the tumor at 90 min post injection. At 19 h post injection the animal was again imaged and tumor visualization was easily obsd. showing specificity of this agent for somatostatin receptors present in this tumor line.

IT 302794-43-ODP, conjugates with cyanine **dyes**

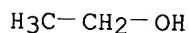
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)

(bioconjugates of cyanine and indocyanine **dyes** with peptides for diagnostic imaging and therapy)

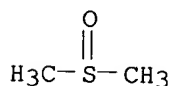
RN 302794-43-0 HCAPLUS  
 CN L-Threonine, D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)



IT 64-17-5, Ethanol, biological studies 67-68-5, Dimethylsulfoxide, biological studies  
 RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (bioconjugates of cyanine and indocyanine **dyes** with peptides for diagnostic imaging and therapy)  
 RN 64-17-5 HCAPLUS  
 CN Ethanol (9CI) (CA INDEX NAME)

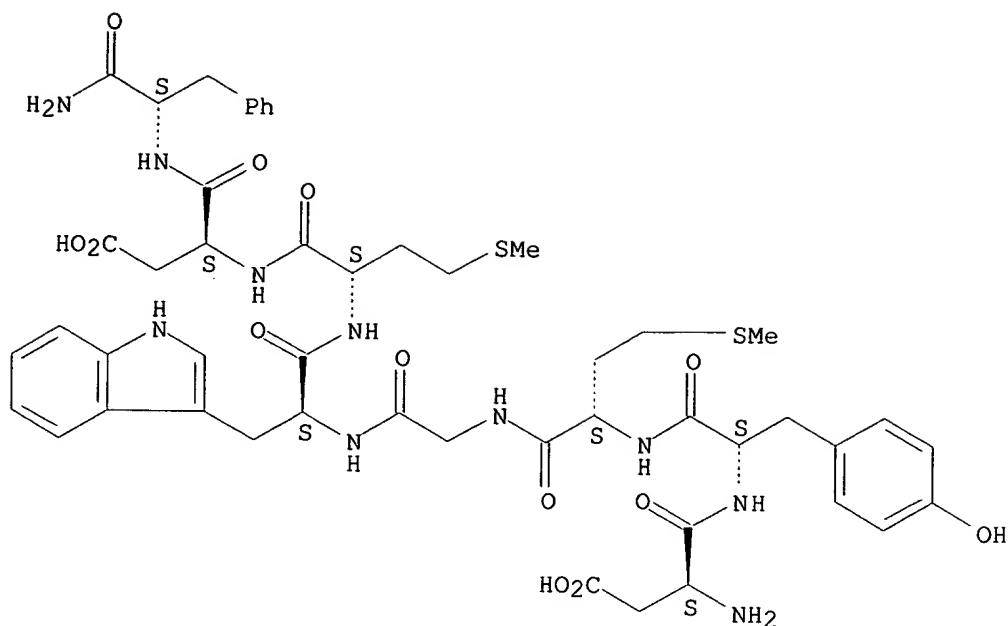


RN 67-68-5 HCAPLUS  
 CN Methane, sulfinylbis- (9CI) (CA INDEX NAME)

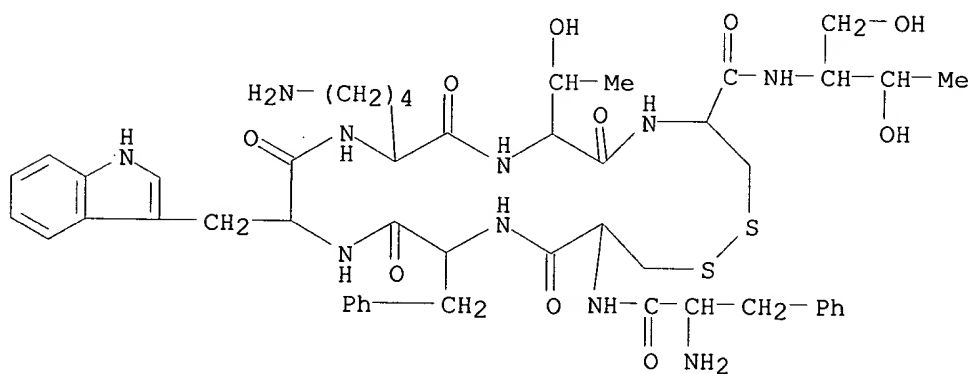


IT 25679-24-7P 83150-76-9P, Octreotide 105466-87-3P 195825-84-4P 302794-43-0P 309916-88-9P 309916-89-0P 309916-90-3P  
 RL: PNU (Preparation, unclassified); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)  
 (bioconjugates of cyanine and indocyanine **dyes** with peptides for diagnostic imaging and therapy)  
 RN 25679-24-7 HCAPLUS  
 CN Cholecystokinin-8 (swine), 2-desulfo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

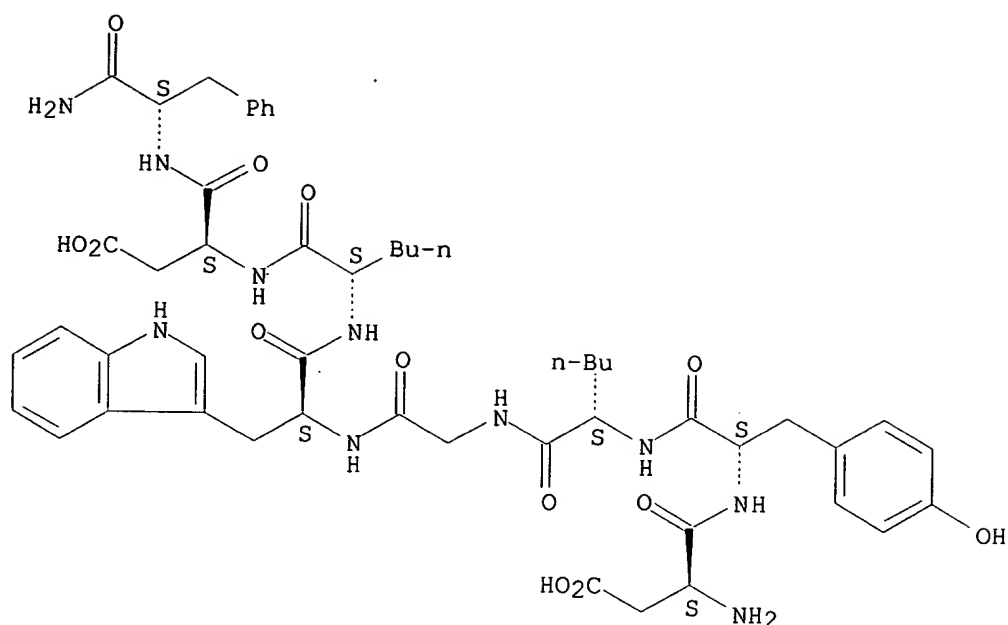


RN 83150-76-9 HCAPLUS  
 CN L-Cysteinamide, D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)



RN 105466-87-3 HCAPLUS  
 CN L-Phenylalaninamide, L-.alpha.-aspartyl-L-tyrosyl-L-norleucylglycyl-L-tryptophyl-L-norleucyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

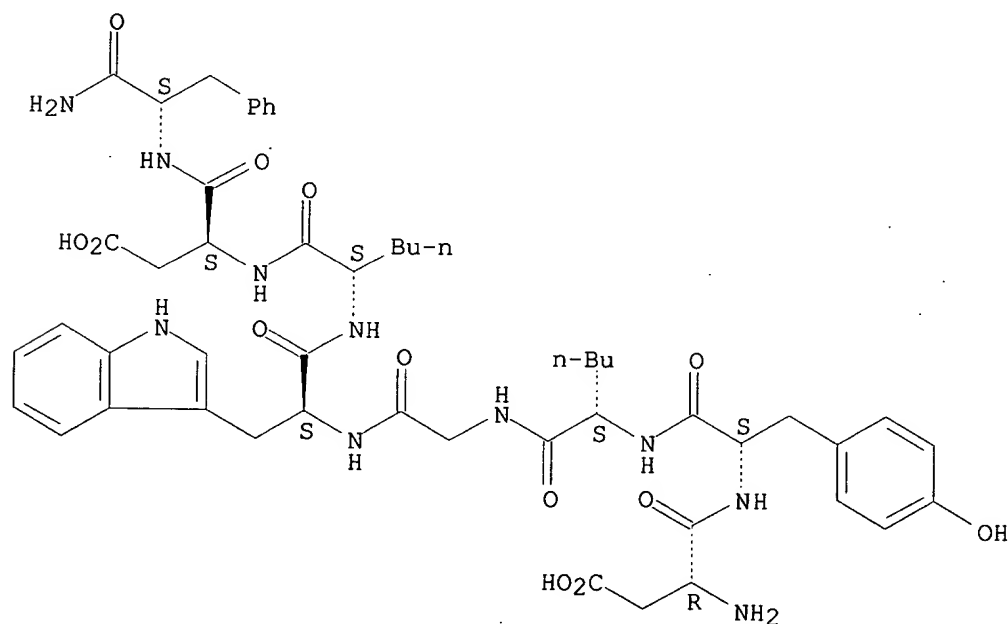
Absolute stereochemistry.



RN 195825-84-4 HCAPLUS

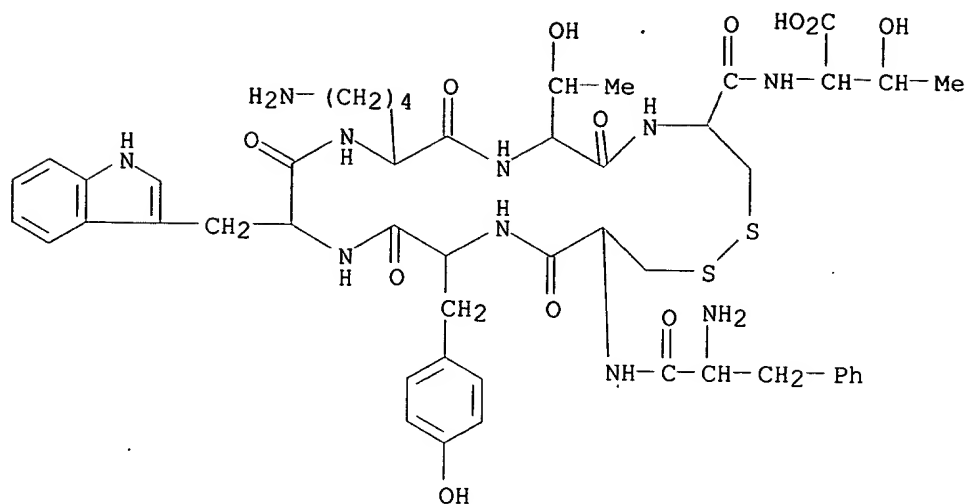
CN L-Phenylalaninamide, D-.alpha.-aspartyl-L-tyrosyl-L-norleucylglycyl-L-tryptophyl-L-norleucyl-L-.alpha.-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 302794-43-0 HCAPLUS

CN L-Threonine, D-phenylalanyl-L-cysteiny-L-tyrosyl-D-tryptophyl-L-lysyl-L-threonyl-L-cysteinyL-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)

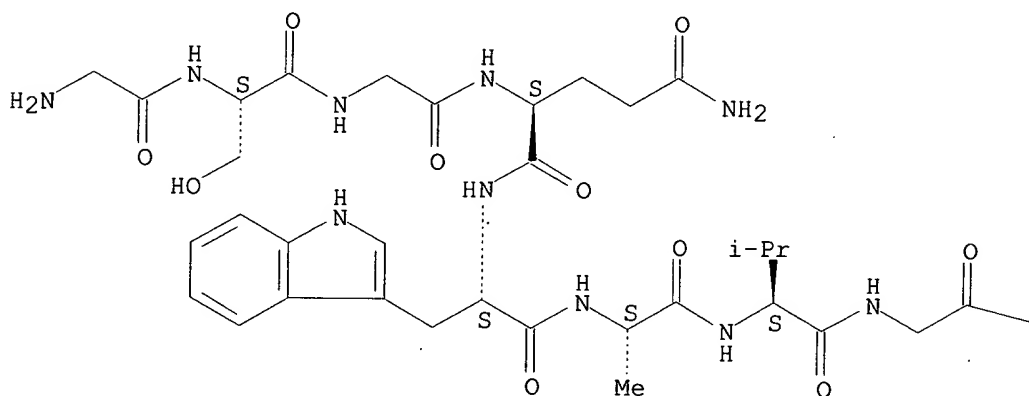


RN 309916-88-9 HCAPLUS

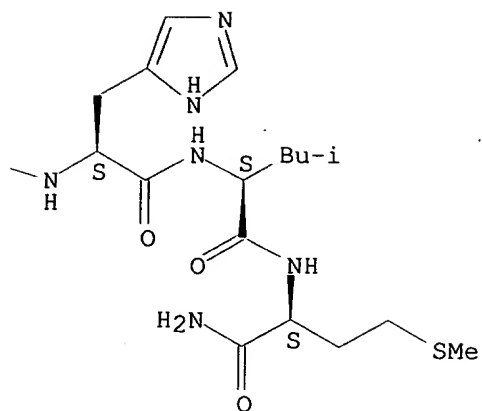
CN L-Methioninamide, glycyl-L-serylglycyl-L-glutaminyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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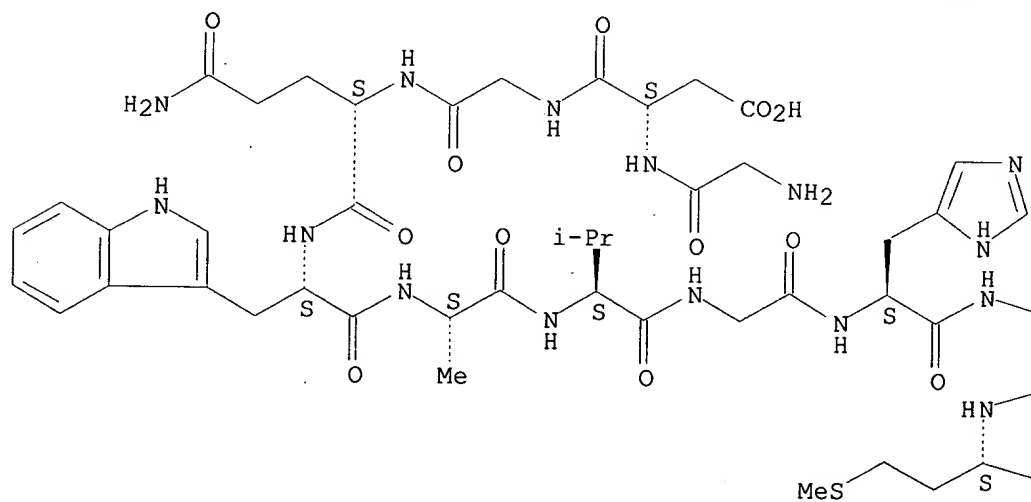


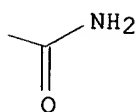
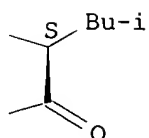


RN 309916-89-0 HCAPLUS

CN L-Methioninamide, glycyl-L-.alpha.-aspartylglycyl-L-glutamyl-L-tryptophyl-L-alanyl-L-valylglycyl-L-histidyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



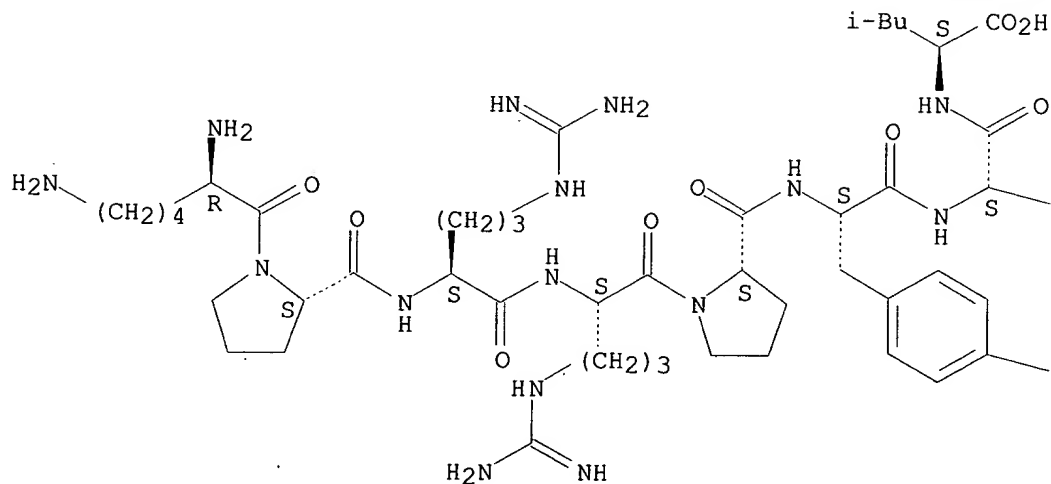


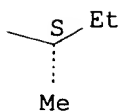
RN 309916-90-3 HCAPLUS

CN L-Leucine, D-lysyl-L-prolyl-L-arginyl-L-arginyl-L-prolyl-L-tyrosyl-L-isoleucyl- (9CI) (CA INDEX NAME)

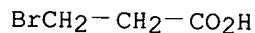
Absolute stereochemistry.

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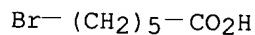




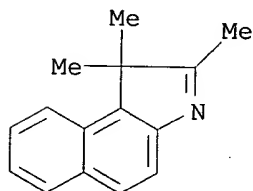
IT 590-92-1, 3-Bromopropanoic acid 4224-70-8,  
 6-Bromohexanoic acid 41532-84-7, 1,1,2-Trimethyl-[1H]-  
 benz[e]indole 309916-91-4 309916-92-5  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (bioconjugates of cyanine and indocyanine **dyes** with peptides  
 for diagnostic imaging and therapy)  
 RN 590-92-1 HCAPLUS  
 CN Propanoic acid, 3-bromo- (9CI) (CA INDEX NAME)



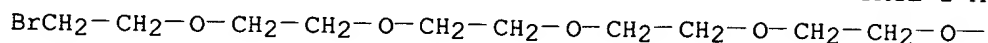
RN 4224-70-8 HCAPLUS  
 CN Hexanoic acid, 6-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



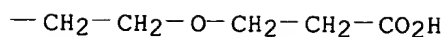
RN 41532-84-7 HCAPLUS  
 CN 1H-Benz[e]indole, 1,1,2-trimethyl- (9CI) (CA INDEX NAME)



RN 309916-91-4 HCAPLUS  
 CN 3,6,9,12,15,18-Hexaoxaheneicosan-21-oic acid, 1-bromo- (9CI) (CA INDEX NAME)

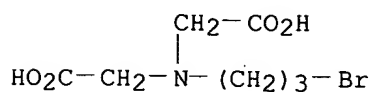


PAGE 1-B



RN 309916-92-5 HCAPLUS

CN Glycine, N-(3-bromopropyl)-N-(carboxymethyl)- (9CI) (CA INDEX NAME)



IT 9011-97-6DP, Cholecystokinin, conjugates with cyanine **dyes**  
 31362-50-2DP, Bombesin, conjugates with cyanine **dyes**  
 37221-79-7DP, Vasoactive intestinal peptide, conjugates with  
 cyanine **dyes** 39379-15-2DP, Neurotensin, conjugates  
 with cyanine **dyes** 51110-01-1DP, Somatostatin,  
 conjugates with cyanine **dyes** 83150-76-9DP, Octreotide,  
 conjugates with cyanine **dyes**  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
 study); PREP (Preparation); USES (Uses)  
 (bioconjugates of cyanine and indocyanine **dyes** with peptides  
 for diagnostic imaging and therapy)

RN 9011-97-6 HCAPLUS

CN Cholecystokinin (8CI, 9CI) (CA INDEX NAME)

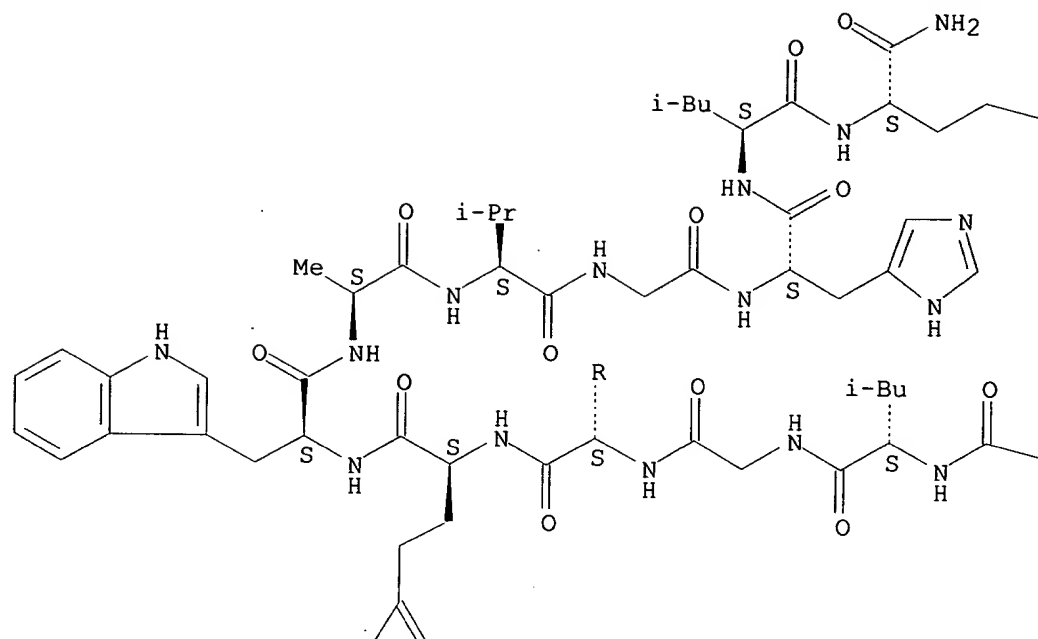
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 31362-50-2 HCAPLUS

CN Bombesin (9CI) (CA INDEX NAME)

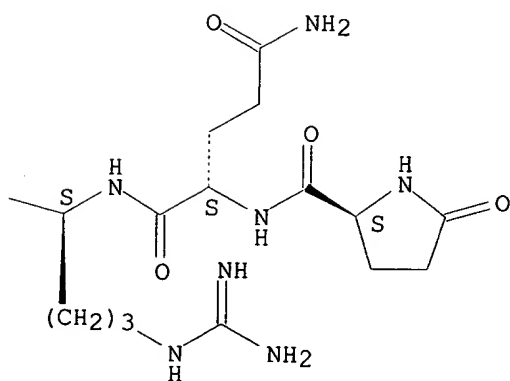
Absolute stereochemistry.

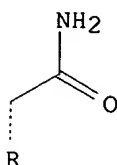
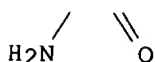
PAGE 1-A



PAGE 1-B

SMe





RN 37221-79-7 HCAPLUS

CN Vasoactive intestinal polypeptide (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 39379-15-2 HCAPLUS

CN Neurotensin (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

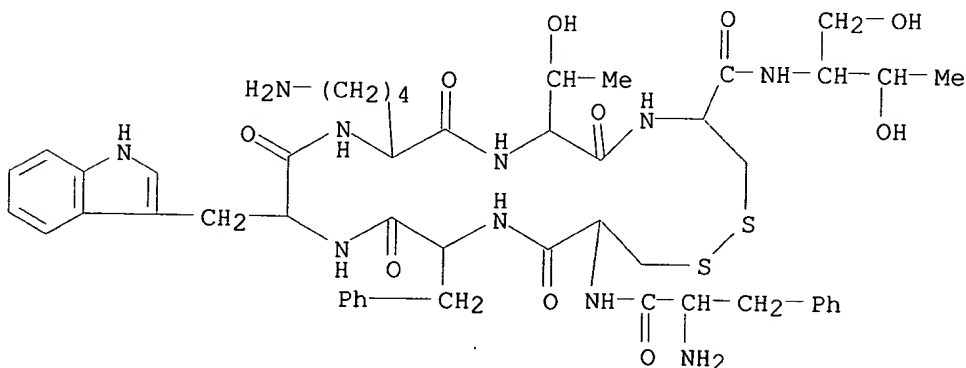
RN 51110-01-1 HCAPLUS

CN Somatostatin (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 83150-76-9 HCAPLUS

CN L-Cysteinamide, D-phenylalanyl-L-cysteinyl-L-phenylalanyl-D-tryptophyl-L-lysyl-L-threonyl-N-[(1R,2R)-2-hydroxy-1-(hydroxymethyl)propyl]-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)

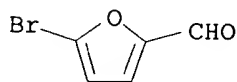


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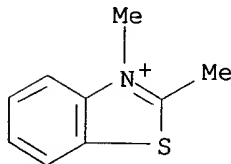
L14 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:157342 HCAPLUS  
 DOCUMENT NUMBER: 128:215272  
 TITLE: Monocyclic functional **dyes** for contrast enhancement in optical imaging  
 INVENTOR(S): Fung, Ella Y.; Rajagopalan, Raghavan  
 PATENT ASSIGNEE(S): USA  
 SOURCE: U.S., 5 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5723104	A	19980303	US 1996-645305	19960513

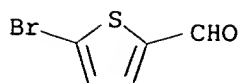
OTHER SOURCE(S): MARPAT 128:215272  
 AB The prepn. and uses of cyanine **dyes** with desirable **photophys.** and targeting properties in imaging of biol. tissues are described. Thus, dimethylbenzothiazolium monocarbothiphen iodide was prepd. by the reaction of 5-bromo-2-thiophenecarboxaldehyde with 1,2-dimethylbenzothiazolium iodide.  
 IT 1899-24-7 2785-06-0 4701-17-1  
 204317-03-3  
 RL: RCT (Reactant)  
 (prepn. of monocyclic functional **dyes** for contrast enhancement in optical imaging)  
 RN 1899-24-7 HCAPLUS  
 CN 2-Furancarboxaldehyde, 5-bromo- (9CI) (CA INDEX NAME)



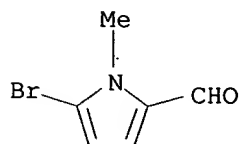
RN 2785-06-0 HCAPLUS  
 CN Benzothiazolium, 2,3-dimethyl-, iodide (8CI, 9CI) (CA INDEX NAME)

● I<sup>-</sup>

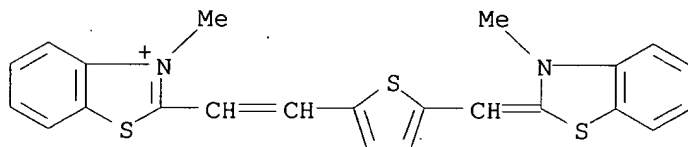
RN 4701-17-1 HCAPLUS  
 CN 2-Thiophenecarboxaldehyde, 5-bromo- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 204317-03-3 HCAPLUS  
CN 1H-Pyrrole-2-carboxaldehyde, 5-bromo-1-methyl- (9CI) (CA INDEX NAME)

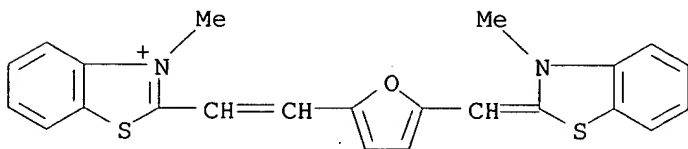


IT 204317-00-0P 204317-01-1P 204317-02-2P  
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of monocyclic functional **dyes** for contrast enhancement in optical imaging)  
RN 204317-00-0 HCAPLUS  
CN Benzothiazolium, 3-methyl-2-[2-[5-[(3-methyl-2(3H)-benzothiazolylidene)methyl]-2-thienyl]ethenyl]-, iodide (9CI) (CA INDEX NAME)



● I<sup>-</sup>

RN 204317-01-1 HCAPLUS  
CN Benzothiazolium, 3-methyl-2-[2-[5-[(3-methyl-2(3H)-benzothiazolylidene)methyl]-2-furanyl]ethenyl]-, iodide (9CI) (CA INDEX NAME)



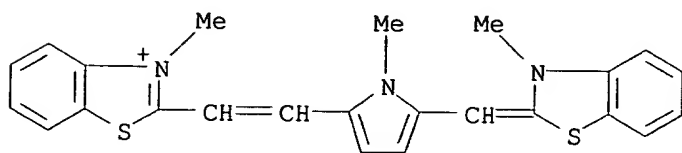
● I<sup>-</sup>

RN 204317-02-2 HCAPLUS  
CN Benzothiazolium, 3-methyl-2-[2-[1-methyl-5-[(3-methyl-2(3H)-



CEPERLEY 09/898,885

benzothiazolylidene)methyl]-1H-pyrrol-2-yl]ethenyl]-, iodide (9CI) (CA  
INDEX NAME)



● I<sup>-</sup>